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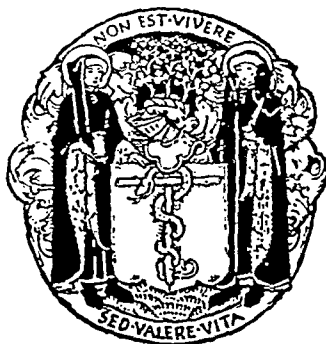
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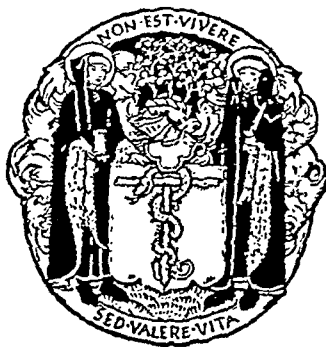
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Section of Comparative Medicine

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[October 18, 1944]

A Half-Century of Serology

PRESIDENT'S ADDRESS

By H. J. PARISH, M.D.

THE time about the year 1894 was a remarkable era in preventive medicine. The discovery of bacteria during the previous two decades had been followed by research into disease-mechanisms, including the study of toxins, and in 1890 Behring and Kitasato had given the world the first inkling of an antitoxin. They showed that the serum of animals that had received non-lethal doses of diphtheria or tetanus toxin could neutralize the corresponding toxin and so prevent its harmful effects. On Christmas Day, 1891, a child in von Bergmann's clinic in Berlin was the first patient to be treated with diphtheria antitoxin; she recovered. During the next three years several diphtheria patients received serum in Berlin, but it was the classic paper of Roux (1894) on the excellent results he had obtained in Paris between February and September of that year which first aroused world-wide interest and led to rapid spread of the new treatment.

THE TREATMENT OF DIPHTHERIA IN THE PRE-ANTITOXIN ERA

George Washington (1732-1799), General, Statesman and first President of the United States of America, was thought by some to have died of diphtheria, but more probably his last illness was a streptococcal pharyngitis or acute laryngitis. He was given gargles of "molasses, vinegar and butter" and of "vinegar and sage tea", bled "heavily" four times, and a blister of cantharides was placed on his throat, "his strength meanwhile rapidly sinking"! Fifty years later (about 1850) blood-letting was still used for throat infections which might have been diphtheria, although the amount of blood withdrawn was less than in the time of Washington. Other remedies included tartar emetic, and, after the acute symptoms had passed, drastic purgation with $\frac{1}{2}$ to 1 grain of calomel every one to two hours—for children from 2 to 5 years old (West, 1850). Within the next fifteen years, treatment showed much-needed improvement and was directed to the control of the local lesion and support of the patient's strength; depletion, blisters and all counter-irritants were altogether discontinued.

Bretonneau (1826), the famous clinician of Tours, first recognized diphtheria as a specific infection, which he termed diphthérie (diphtheritis), since modified by his pupil Trousseau to diphthérie (diphtheria). He also performed the first successful operation for tracheotomy. Bretonneau had witnessed the death from diphtheria of three of the four children of a friend, and, as the fourth lay dying also, he sought and received permission to open into the trachea. The patient recovered and lived to the age of 71.

THE MODERN HISTORY OF DIPHTHERIA

The modern history of diphtheria was ushered in by workers in Germany and France, notably Klebs and Loeffler; Behring, Fraenkel and Kitasato; and Roux, Yersin and Martin. The debt we owe to the animal world as a field for experiments and testing must be gratefully acknowledged.

In 1894, the year of Roux's classical paper on the serum treatment of diphtheria, Sir Joseph Lister obtained some of Roux's serum in Paris and gave it to E. W. Goodall, at that time Medical Superintendent of the Eastern Hospital, Homerton, of the Metropolitan Asylums Board, London. The twenty cases Goodall treated with this serum were the first to receive antitoxin in England. In the same year, Armand Ruffer prepared antitoxin at the British Institute of Preventive Medicine, now the Lister Institute, and his serum also was first used by Goodall at the Eastern Hospital on October 23. The Wellcome Physiological Research Laboratories were originally established in London in 1894, and serology became an important part of their activities soon afterwards.

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the rapid elimination of toxoid after injection, and showed that the increased efficiency of alum precipitated toxoid (A.P.T.) was due to slow absorption and elimination. This discovery of the value of alum, together with Glenny's emphasis on the proper spacing of doses so as to encourage a "secondary stimulus response", has been invaluable in the preparation of antiserum in horses and in active immunization in man.

Progress in standardization.—The development of improved antigens must go *pari passu* with improvements in methods of standardization in the laboratory. We have seen how Ehrlich (1897) first introduced methods of exact measurement into the new science. It is said that he spoke scathingly of Behring because he had ignored or at least failed to develop logically the quantitative aspects of serology. Be that as it may, Ehrlich was pre-eminent as a laboratory investigator; he was, in fact, the first great immunologist. Until 1909 most animal experiments involved subcutaneous injections, but in that year Römer gave a fillip to investigations of blood antitoxin in man and animals by introducing his intradermal diphtheria virulence test in guinea-pigs was developed through the stimulus of Römer's discovery, and so also was the Schick test (1913) which provides a clinical method for determining immunity to diphtheria, based on the antitoxin content of the blood. By the way, Schick testing was introduced in this country as a public service, at the Infant Welfare Centre in Holborn, London.

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Enzyme-treated sera represent a great advance on the older types of antitoxin prepared by salting-out methods. A greater degree of purity is obtained; there is a marked increase in the number of units of antitoxin per gram of protein; and the antitoxic molecule is altered, being approximately half the size of the molecule in natural serum or in serum concentrated by the older method of ammonium sulphate precipitation.

At the commencement of 1895 diphtheria antitoxin was on its trial throughout the whole civilized world, and between 1895 and 1899 there was a great diminution in the hospital case mortality rates as a result of antitoxin therapy. Towards the end of the last century, too, quantitative methods of titration were being introduced, and serology was becoming an exact science; Paul Ehrlich made his principal communication on the standardization of diphtheria toxin and antitoxin in 1897.

In tracing broadly the origin and development of ideas, I shall try to indicate why things were done in a certain way at a certain time and what led to modifications of methods and to new discoveries. In 1884, Loeffler killed animals with cultures of diphtheria bacilli and suggested but did not prove that the organism caused death by elaboration of a toxin. In 1888, Roux and Yersin proved the existence of this toxin; culture filtrates injected into animals caused death in exactly the same manner as the living bacilli themselves. How was antitoxin discovered? In 1890, Behring and Kitasato noted that the serum of animals which had been injected with non-lethal doses of diphtheria and tetanus toxins had acquired a new property, viz. something which could neutralize or prevent the harmful effects of lethal doses of the toxins. Much of the early work was done in rabbits, but it was quickly realized that if antitoxin was to be used in the treatment of human beings serum would have to be acquired from large animals, particularly horses. The injection of gradually increasing amounts of toxin into animals was soon found to be an unpractical method of producing antitoxin, because of the very severe reactions produced. Behring and Wernicke, about 1892, showed that animals could be immunized by increasing doses of living cultures after a protective dose of antitoxic serum. From this point, it is a small step to the immunization of animals by injections of toxin partially neutralized by antitoxin, so-called toxin-antitoxin mixtures. Park (1929) has stated that as early as 1897 he used such mixtures for horses in New York City which were used to produce diphtheria antitoxin, and in 1903 he published records showing that three such injections might produce several hundred units of antitoxin per cubic centimetre of serum. Theobald Smith, in 1909, was the first to suggest the use of toxin-antitoxin injections for the active immunization of children.

One method of producing antitoxin in animals and man was thus the use of preparations containing toxin, the serious effects of large doses of which were mitigated by partial neutralization with antitoxin. Another line of investigation was to modify toxin itself so that it could be rendered non-toxic or harmless on injection, while retaining its antigenicity. Salkowski first described, in 1898, the interesting method of modifying toxin with formalin, and in 1904 both Loewenstein in Vienna and Glenny in England were using formalinized toxin, now known as toxoid, in their work. Glenny (personal communication) first produced toxoid by accident. In those days formalin was added to the butts in the diphtheria toxin laboratory as part of the sterilization process between successive batches. Sometimes a particular batch of toxin was of low value when tested for minimum lethal dose and combining power in guinea-pigs, but yet immunized animals as satisfactorily as the much more lethal batch which preceded it. The explanation of the anomaly was that the residual formalin in the bulk container had converted some of the toxin into toxoid.

Although toxoid was in use in serological laboratories in 1904, about twenty years were to pass before it was used for human immunization (O'Brien, 1925). Glenny, Allen and Hopkins first suggested this field of investigation in 1923, and Ramon first put the method into practice in that year, closely followed by Nash, M.O.H. for Heston and Isleworth, in London. In 1924 toxoid was being used fairly extensively in France, under the name of "anatoxine".

Diphtheria immunization of man received a serious setback by the disasters at Dallas in 1919, Concord in 1924 and Baden in 1925, when toxic preparations were injected instead of properly balanced mixtures of toxin and antitoxin. Although adequate and complete reasons were given to account for these misfortunes, it was only to be expected that toxin-antitoxin mixtures were henceforth doomed for human immunization. In this country toxoid-antitoxin mixtures were already in use in 1924 and 1925, but were superseded to a large extent during the next decade by two more potent antigens, toxoid-antitoxin floccules (T.A.F.) and alum precipitated toxoid (A.P.T.). In 1925, Hartley of the National Institute for Medical Research, Hampstead, prepared toxin-antitoxin floccules which produced immunity in animals, and two years later Glenny and Pope advocated for human use toxoid-antitoxin floccules—suspensions of the floccules which form when toxoid and antitoxin are mixed in certain proportions. In 1926 Glenny, Pope, Waddington and Wallace discovered that the antigenic value of toxoid was enhanced by the addition of alum. An insoluble compound was produced which remained in the tissues and afforded a prolonged stimulus. Five years later Glenny and Barr (1931) recommended washed alum toxoid precipitates as antigens. Glenny, Buttle and Stevens (1931) demonstrated

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[The President concluded his Address by showing on the epidiascope portraits of many of the pioneers in the field of serology, beginning with Robert Koch, for it was two of his pupils, Behring and Kitasato, who first discovered antitoxic sera. The series of portraits was accompanied by brief biographical notes and formed a most interesting supplement to the Address.]

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Section of the History of Medicine

President—Sir WALTER LANGDON-BROWN, M.D.

[June 7, 1944]

Edward Bancroft, M.D., F.R.S., and the War of American Independence.

By Sir ARTHUR S. MACNALT, K.C.B., M.D., F.R.C.P.

CONAN DOYLE in the *Adventure of the Noble Bachelor* puts the following words into the mouth of Sherlock Holmes:

"It is always a joy to me to meet an American, for I am one of those who believe that the folly of a Monarch and the blundering of a Minister in far gone years will not prevent our children from being some day citizens of the same world-wide country under a flag which shall be a quartering of the Union Jack with the Stars and Stripes."

To-day when Britons and Americans are fighting side by side once more to preserve freedom and civilization, we are overjoyed to meet an American, and this afternoon I want to introduce you to one whose advice if taken might have helped to make that world-wide country in the eighteenth century.

Edward Bartholomew Bancroft, for many years forgotten, has many claims on our notice as physician, eminent scientist, philosopher, politician, novelist, technical expert in dyes and philanthropist. But it was not until seventy years after his death that he was also discovered to be the most remarkable spy of all time.

He was born at Westfield, Massachusetts, in 1744. The Bancrofts came of good yeoman stock and are a well-known family in Massachusetts. The founder of the family was John Bancroft who came there in 1632. John's grandson, Samuel, was born at West Springfield, Massachusetts, in 1768 and removed to Granville in the same State. He may have been a cousin of Edward's for the latter called one of his own sons Samuel. Distinguished Bancrofts were the Rev. Aaron Bancroft (1755-1839), Unitarian divine and author of a life of Washington (1807), George Bancroft (1800-1891), the historian and United States Minister to Great Britain, Hubert Howe Bancroft (1839-1901), a great educationalist. Professor Wilder Bancroft is Emeritus Professor of Chemistry in Cornell University. Thus Edward belonged to an illustrious New England family. As a boy he was apprenticed to a trade. Running away while in debt to his master, he became a sailor and made several voyages. On his return he paid what he owed. Like Franklin, he was largely self-taught, but he appears to have gone to school, perhaps at Groton, Connecticut, in 1758, for Silas Deane, a native of that town, was one of his teachers.

He next seems to have acquired some medical training, possibly as a surgeon's mate on board ship, for we find him as a medical attendant on a West Indian plantation and later in a similar capacity in Dutch Guiana (Surinam). Here Bancroft met Paul Wentworth, a member of a well-known New Hampshire family, who owned a plantation there and who greatly influenced his career afterwards. Bancroft took advantage of his post to study the flora and fauna of Guiana and early gained reputation as a botanist and zoologist. His researches were recorded in his first published book, *The Natural History of Guyana* (1769), written in the form of letters to his brother. He also studied tropical plants and their dye-producing properties.

[The President concluded his Address by showing on the epidiascope portraits of many of the pioneers in the field of serology, beginning with Robert Koch, for it was two of his pupils, Behring and Kitasato, who first discovered antitoxic sera. The series of portraits was accompanied by brief biographical notes and formed a most interesting supplement to the Address.]

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in Paris as a joint commission. Lee suspected Bancroft of being a spy, but had no proof. To counter this, Bancroft arranged with William Eden, Under-Secretary of State, that he should be arrested on a charge of complicity in the plot of "John the Painter", John Aitken, for setting fire to British dockyards and exiled to Paris, where Franklin made him Secretary to the American Commission. In this way the British Government had access to all the secrets and plans of Congress and the Commissioners. Bancroft, under his secret agent name of "Mr. Edwards", throughout 1777 repeatedly implored the Government to make peace with the Colonies before their alliance with France was concluded. Had his advice been taken, a durable settlement might have been made and many thousands of British and American lives spared.

Unfortunately, King George III shut his eyes to the impending danger, writing to Lord North that "as Edwards is a stockjobber as well as a double spy, no other faith can be placed in his intelligence, but that it suited his private views to make us expect the French Court means war". Bancroft held up the information of Burgoyne's surrender at Saratoga in order to make "a killing on the London Stock Exchange", and netted a large sum by his astuteness. This confirmed the King's distrust. When the Treaty of Alliance between France and the United States was signed in 1778, Bancroft transmitted a copy of it to the British Government within the unprecedented short space of forty-two hours.

During the concluding years (1780-83) of the War of American Independence Bancroft continued to render good service to the British Cause. He supplied all particulars concerning the French fleets and armies to the Government. His position as Secretary to the Commissioners was so well established that de Vergennes in 1779 sent him to Ireland in order to survey the prospects of fomenting an insurrection in Ulster with aid from France. Bancroft advised against this scheme, and in 1780 his salary as a British agent was increased from £500 to £1,000 per annum. Nor was the indefatigable Doctor unmindful of his business interests. In this year, Paul Jones entered into a commercial enterprise with him for importing quercitron bark for dyeing wool. Berthollet in his *Elements of the Art of Dyeing* (1791) tells us that Dr. Bancroft had obtained an exclusive right to the traffic of this bark in France as well as in England. His agent in France was a "Mr. Brown," evidently a respected authority on dyeing.

In 1783 the Whig Ministry acknowledged the independence of America and a treaty was signed by the Americans without the knowledge of their French allies. In September general peace was restored. Bancroft, no doubt, was closely concerned as an intermediary behind the scenes in all these negotiations.

In June 1783 he saw Lord North and Mr. Fox in London and arranged to get information for them concerning the state of affairs in the United States. He ostensibly went there on a mission to recover payment of a loan which had been made by the Prince of Luxemburg to the State of South Carolina. He stayed with his friend Franklin in Philadelphia and obtained much political information which, on his return in 1784, he gave to the British Government. He had an interview with Mr. Pitt in which he advised a naval blockade of America, asserting if this were done that within a year the Colonies, finding their trade interests thus affected would return to their old allegiance. But the British Government had had enough of fraternal warfare.

It was at this time that Bancroft wrote his striking appeal to the Marquis of Carmarthen, Foreign Secretary, for arrears of salary in which he records his services as a British spy. This apparently wound up his employment in the British Intelligence Service and he proceeded thereafter with his researches in the chemistry of dyeing and with his commercial and speculative ventures. He retained his British citizenship, and in 1785 an Act of Parliament was passed concerning the discovery of quercitron bark, the use and application of which for dyeing, calico-printing, &c., were exclusively vested in Dr. Edward Bancroft for a term of ten years, in addition to his original monopoly of fourteen years, making twenty-four in all. This was procured by Government interest and evidently as a solatium to the ex-spy, for Mr. Eden was active in carrying the Bill through the House of Commons. He still retained an interest in affairs and oscillated between London and Paris from 1784 to 1792 keeping his finger in the British and American political pie.

Although a fortune must have passed through his hands, Bancroft was often pressed for money. He had a growing family to support, two establishments, one in London, the other in Paris, and his business enterprises involved him in expensive litigation. Yet he had a kind heart, and when the unjustly discredited Silas Deane wrote to him from Ghent, Bancroft invited him to London and helped him with money and medical care. Deane died in 1789 at Deal on the eve of departure for Canada and Bancroft wrote the account of his end.

He urged Franklin to write his autobiography. In 1786 Franklin wrote to Bancroft: "I have made some progress in my autobiography and hope to finish it this winter". In

comparatively recent times. He adds: "In fact, I believe it is still used to a small extent. At any rate, it was advertised and listed in trade directories until the outbreak of war."

At 30 years of age then, Edward Bancroft was settled in London, married, a Fellow of the Royal Society and with a high scientific reputation. In starting manufactures of calico printing and woollen dyed goods he was turning his botanical and chemical knowledge to profitable use. His industry must have been indefatigable, for these multifarious occupations did not solely occupy the time of the young American. These were the days when the colonists of North America were beginning to stretch their limbs and realize that the mother country could no longer keep them in leading strings.

Edward Bancroft appeared now as an American patriot. He published in London, in 1769, *Remarks on a Review of the Controversy between Great Britain and Her Colonies*. This essay was a noteworthy contribution towards a possible settlement. He attended with his friend Benjamin Franklin the famous meeting in the Cockpit in 1774, when Franklin was arraigned before the Privy Council Lords Committee, and renewed his friendship with Paul Wentworth, now an American agent of the British Intelligence Service. The latter induced Bancroft to take up the hazardous and perilous role of a double spy.

In 1775 Paul Revere made his famous ride and hostilities between British troops and the Colonists began with the disastrous affair at Lexington. Franklin in that year returned to America, and in June 1776, Silas Deane came to Paris as the first diplomatic representative of the United States. He carried with him Franklin's instructions and letters to Bancroft. Bancroft saw Deane in Paris, learned the purpose of his mission and his secret negotiations with the French Government. In a memorial to the Marquis of Carmarthen (1784) which is among the Auckland Papers in the British Museum, Bancroft states that he had then resided ten years in England and expected to spend the rest of his life there. He felt as a loyal British subject that the Government should be informed of the danger of French interference and hoped that thus informed they would prevent it by some accommodation with the Colonies or by other means. He emphasizes that his motives at the outset were purely disinterested. On his return to England, Bancroft consulted Wentworth who took him to see the Secretaries of State, Lords Weymouth and Suffolk. These astute noblemen soon realized that in Bancroft they had found a most valuable informant. "I was urged on", writes Bancroft "to watch and disclose the progress of it; for which purpose I made several journeys to Paris, and maintained a regular correspondence with Mr. Deane through the Couriers of the French Government. And in this way I became entangled and obliged to proceed in a kind of Business, as repugnant to my feelings, as it had been to my original intentions." All this is no doubt perfectly true, but he adds: "Being thus devoted to the Service of Government, I consented, like others, to accept such Emoluments, as my situation indeed required."

Mr. Lewis Einstein whose authoritative work, *Divided Loyalties*,¹ treating of Americans in England during the War of Independence, first introduced me to Bancroft, and who has kindly helped me in the preparation of this paper, points out that in a letter to Deane the Doctor had much to say about his influential English friends "like Lord Camden, and Thomas Walpole, the member from Lynn, who at this time, unknown to Deane, was Bancroft's partner in speculations on the Stock Exchange as well as in certain ventures of shipping contraband to America". These are further indications of Bancroft's large business interests, some, I fear, not altogether reputable. He conveyed items of gossip and trivial information about English politics to Deane who accepted them indiscriminately, and wrote to the Secret Committee of Congress in Philadelphia that no one had better intelligence in England than Bancroft who was in close touch with the Whig Opposition. "Dr. Bancroft of London merits much of the Colonies", he added later.

The double rôle of American patriot and British spy was a difficult one to play, but, as we shall see, Bancroft played it to perfection. Both he and Deane were in communication with M. Garnier, the French Chargé d'Affaires in London, and Bancroft was able to send his letters to Deane uncensored to Paris in the French diplomatic pouch. Although this was done with the knowledge and approval of his employer, William Eden, Under-Secretary of State, who controlled the British Intelligence Service, nevertheless Eden distrusted him, and on one occasion when Bancroft's mistress was leaving to meet him in Paris, another American spy, the Reverend John Vardill, supplied her with a companion who secretly examined the letters she carried.

"The Olive Branch Petition" failed, and Congress published the Declaration of Independence. In December 1776, Franklin and "proud and jealous Arthur Lee"² joined Deane

¹ EINSTEIN, L.: *Divided Loyalties. Americans in England During the War of Independence*. Cobden and Sanderson, London, 1933.
² ARTHUR LEE (1740-1792) was born at Stratford, Connecticut. Educated at Eton and Edinburgh University, M.D. Edin. 1764 and F.R.S. 1766. He forsook Medicine for law and was called to the English Bar in 1775. He was appointed agent for Massachusetts in Great Britain in 1770. A.S.M.

procured, were currently sold ("though without any benefit to me") for *six times their original price*.

In 1799 Bancroft failed to get his monopoly for importing quercitron bark renewed; the bill for extension passed the Commons with commendable speed, but was thrown out by the House of Lords owing to organized opposition by Northern dye manufacturers. Bancroft wrote a pamphlet of protest to Parliament upon the subject. He writes in 1813: "I was left with very little remuneration for the labours of a great part of my life. In less than twelve months this bark rose to three times the price at which it had been invariably supplied by me, and at which I should have been bound to supply it for another term of seven years, if the bill had become law; and it has on the average been at nearly double that price to the present time. This is the *only instance*, I believe, in which an invention ever became more *costly* after the expiration of a monopoly, granted to remunerate the inventor, than it was during the continuance thereof, and it has *demonstrated most incontrovertibly*, that my opponents were greatly *deceived* and that I was greatly wronged".

With the idea of compensating himself financially for this disappointment, Bancroft postponed work on the second volume of *The Philosophy of Permanent Colours*, and, although nearly 60 years of age, made two voyages, one to North and the other to South America. We learn from a note to his son's *Essay on Yellow Fever* that in 1804-5 he was in South America and stayed with Dr. and Mrs. Ord when going from Demerary (Demerara) to Berbice in British Guiana and returning thence. Dr. Ord was formerly Surgeon to the 39th Regiment. Bancroft ascertained from him that he did not consider Yellow Fever contagious, and obtained a similar opinion from Mr. Dunkin, late Garrison Surgeon at Demerary and then Deputy Inspector of Army Hospitals. The veteran traveller probably also visited Surinam and renewed old friendships both there and during his tour of the United States. When one remembers the discomforts and perils by land and sea in travelling in the early part of the nineteenth century and the grave risks of contracting yellow fever and malaria in South America, the Doctor's courage and adventurous spirit at a comparatively advanced age call for high commendation. But, as he himself tells us, in both of the two expeditions his expectations of financial success were frustrated by ill-health, and he returned to England "having then attained an age but little suited to a renewal of such undertakings".

He was now an old man. The days of midnight revels in London and Paris were over; political scheming and intrigues were things of the past. Yet his brain still was active, and he pursued his chemical experiments with all the zeal of the true scientist. He must have been cheered by his eldest son's professional distinction. In 1811 he edited this son's *Essay on Yellow Fever*. He supplied a number of footnotes to the book, but does not obtrude himself as editor.

In 1813 Bancroft published a revised first volume and the promised second volume of *The Philosophy of Permanent Colours*. He notes on the title-page that he is a Fellow of the American Academy of Arts and Sciences of the State of Massachusetts Bay. An American edition was published by Thomas Dobson, Philadelphia, in two large octavo volumes, price six dollars. This work had an equally good reception to that given to the volume published in 1794.

The last publication of Bancroft's which I have been able to trace appeared in 1816 in the *Annales de Chemie*, Vol. III, pp. 225-237. It was entitled: "Instruction concernant les préparations nommées 'lac-lake' et 'lac-dye'."

Bancroft's residences in London were various. In 1775 he lived in Downing Street, Westminster. He was probably in practice there as a physician for it was then a doctor's street. Tobias Smollett set up practice there in 1744. In 1785 Bancroft resided in Villiers Street, York Buildings, and in December 1798 at Francis Street, St. Pancras. He also lived at Turnham Green, perhaps originally at the suggestion of Dr. Ralph Griffiths, the Editor of the *Monthly Review*, who had a house there.

Universally respected and honoured, Edward Bancroft died at Margate on September 8, 1821, aged 77 years. Short obituary notices are to be found in the *Gentleman's Magazine* and the *Annual Register* for that year.

As I have said, it was not until seventy years after his death that his activities as a spy became known. His grandson, a General in the British Army, was so distressed by the revelation that he destroyed the greater part of Bancroft's papers and correspondence, thereby inflicting an irreparable loss on the secret history of the American War of Independence.

Dr. Bancroft had several children of whom the eldest, Edward Nathaniel, calls for special notice. He was born in London and educated at Dr. Burney's famous Academy at Hammersmith and under Dr. Parr at Norwich. At the age of 17 he was admitted a

the following year Bancroft collected some of Franklin's *Political and Miscellaneous Papers* and published them in London.

In 1789 John Jay suggested that Bancroft should be appointed an Envoy from the United States to carry out an informal mission to England, but Hamilton preferred that the task should be assigned to Gouverneur Morris, the United States Minister to France. The recently published *Diary of Gouverneur Morris*³ has a number of references to Bancroft, whom Morris met frequently both in Paris and London. We see the genial doctor bustling in, pressing the Minister "to eat a Bit of Mutton with him", recommending a good doctor, one Dr. Jefferies, and a surgeon for Morris's servant, all the while keeping his ears open for any political news or gossip which he can turn to his own advantage. At another time he has a "Certificate of Pensilvania to sell" or news about Lord Grenville asking the Hon. Thos. Walpole to go out to America. He gives a scientific dinner-party in London to which he invited Morris. The famous Dutch physician, Dr. John Ingenhousz, was another guest. On March 4, 1792, Morris notes: "Dine with Dr. Bancroft and go afterwards to Governor Franklin's where we play whist till very late". There are less edifying accounts of revels in Paris in 1791 when Morris dines with Bancroft and his mistress, or when he takes Bancroft and his friend, Mrs. Rose, to the opera.

Gouverneur Morris also acted as an intermediary between Paul Jones and Bancroft in the winding up of their partnership in the dyeing business (1790). Throughout the year 1792 Bancroft was chiefly engaged in preparing for the Press the first volume of his *magnum opus*. This was entitled *Experimental Researches Concerning the Philosophy of Permanent Colours and the Best Means of Producing Them by Dying, Callico Printing, &c.* by Edward Bancroft, M.D., F.R.S., Vol. I, 1794. Printed for T. Cadell, Jun., and W. Davies in the Strand.

In the preface he says a second volume is intended to follow. "That and the present volume will contain the results of many thousands of experiments and of much observation and reflection during the space of twenty-five years, in which this subject has been my principal occupation; and as it will probably continue to occupy a greater part of my time, whilst life and health are prolonged to me, I may be allowed to hope, that future discoveries will hereafter enable me to publish at least one other volume as supplementary to these, which are intended to convey all the knowledge I have hitherto acquired on this subject."

Von Meyer in his *History of Chemistry* states that the early scientific chemists endeavoured not only to prepare and apply colours by practical recipes, but also to aid the manufacturer by speculations upon the modes in which dyeing processes are brought about. Dyes were divided by them into two classes, according as they were capable of being fixed upon cloth with or without mordants, and Bancroft distinguished these as *adjective and substantive dyes*.

Bancroft's work thus constituted a valuable introduction to the chemical industries of to-day. His account of the scarlet dye "Barry Red" (cochineal), his mordant for quercitron bark in the woollen dye and his discovery of a mordant for dyeing with Prussian blue may be specially singled out for notice. His book became the standard British and American authority on the subject of dyeing, though Thomas Packer in *The Dyer's Guide* (1816) says: "Bancroft is too expensive and voluminous for an introductory work". Thomas Cooper, Professor of Chemistry in Dickinson College, Carlisle, Pennsylvania, in his book, *A Practical Treatise on Dyeing and Callicoe Printing*, published in 1815, observes in his preface: "Bancroft, who having discovered and secured a monopoly of the bark of the American black oak, turned his attention to dyeing, has published a very valuable treatise, but not a practical one. The history and description of the drugs used, and the theory that pervades the book is excellent". He adds that if he were a dyer and a young lad was sent to him to be instructed in the art he would first expect of him a good knowledge of the elements of chemistry. "I should then instruct him in the materials used in the art of dyeing. Bancroft's book to which mine is a practical supplement would do this better than any other".

Mr. Lawrence Morris writes to me: "Bancroft's book *The Philosophy of Permanent Colours*, was the first important work on dyeing and dyestuffs in the English language. It remained of considerable value and was widely read up to the time of the discovery of the first coal-tar dyestuffs in the 'fifties' and 'sixties' of the last century, and for long after".

In this work Bancroft displays his profound knowledge for those days of applied chemistry and of botany. The book had a ready sale. The edition of a thousand copies was soon exhausted and Bancroft mentions that second-hand copies, when they could be

³ *A Diary of the French Revolution*, by GOUVERNEUR MORRIS, 1782-1816, Minister to France during the Terror, edited by Beatrix Cary Davenport, 2 vols., G. G. Harrap and Co., Ltd., London, 1939.

Auckland papers were published, said that if Bancroft were really a spy he presents a case of which history affords no parallel. He wrote: "To believe him guilty of such atrocious and yet exquisitely subtle perfidy we must believe that ingenuous, simple-hearted and credulous as he appeared to the general observer . . . he was, nevertheless, a dissembler so artful as to defy the scrutiny of Franklin, with whom he was in constant intercourse, an intriguer so skilful as, without money or power, to deceive Vergennes and the multitudinous police with which Vergennes encircled him; a villain so profoundly wary as to win the confidence of Paul Jones, professedly aiding him in desperate secret raids on the British coast, and yet, by an art almost unfathomable, reserving the disclosure of these secrets to British officials . . . ; a double traitor, whose duplicity was so masterly as to be unsuspected by the British Court, which held him to be a rebel; and by such men as Lafayette, as John Adams, as Jefferson, who regarded him as a true friend".

Dr. Wharton's defence has proved to be the most scathing description of Edward Bancroft's double-dealing. On this aspect of Bancroft's character, I can only urge that as a spy he took his life in his hands, as he well realized; that he was consistently loyal as a British secret agent; and that he gave full and reliable information and advice to the British Government, advice which if followed might have brought about an honourable and peaceful settlement between Great Britain and America at an early stage of the War of Independence. A man who becomes a spy from patriotic motives without hope or desire of reward may deserve commendation. Bancroft had extravagant tastes and his besetting temptation was money getting. His engaging in shipping of contraband from Britain to America, his holding up of the news of Burgoyne's defeat to make that "killing on the London Stock Exchange", and his acceptance of a salary from both sides can hardly be defended. These sins brought their own punishment, for George III thoroughly distrusted him.

Another defect in his character was that he frequently laboured under a grievance. He was, as Wentworth said, "most difficult to handle".

In the hazardous occupation of a spy he was never found out, and he retained the friendship and even affection of both British and Americans.

He warmed both hands at the fire of life and probably got a good deal of satisfaction out of his adventurous and speculative career. He publicly avowed that "every part of animated nature was created for its own happiness only", and he lived up to that belief.

John Zephaniah Holwell (1711-1798) and the Black Hole of Calcutta

By H. P. BAYON, M.D.

THE lack of fresh air in closely black-out halls and recent tragic disasters in deep shelters may recall the deaths in the "Black Hole" of Calcutta, June 20-21, 1756. This terrible event occurred barely two centuries ago; even so, several essential details are no longer ascertainable, but there is a first hand account by one of the survivors, the surgeon John Zephaniah Holwell.

Though, at the time, John Mayow (1643-79) and his several precursors had published their experiments on respiration and Stephen Hales (1677-1761) described his ventilators to the Royal Society in May 1741, still there was very little knowledge of the intricacies of the physiology of breathing in general and of the vital necessity for ventilation of closed spaces in particular. Understanding began with the discoveries of Lavoisier (1743-94), whose pioneer work was clarified by Pierre Simon Laplace (1749-1827), Joseph Louis Lagrange (1736-1813) and Jean Henri Hassenfratz (1755-1825) and many others besides—then and since—for the subject is still being actively and fruitfully studied.

Thus Holwell's report can now be read in the light of modern experience.

THE ATTACK ON CALCUTTA BY MIRZA MAHMOUD

In 1756 the garrison of Fort William, Calcutta, consisted of about 180 soldiers of whom a third were English, the remainder Sepoys or Indians. When the Nawab of Bengal, Mirza Mahmoud, Siraj-ud-Dowlah, a young man of eighteen, ordered his troops to attack the British settlement, the Governor, Roger Drake, abandoned the post with his retinue and sought refuge on board a ship; he was eventually, though tardily, charged

sizar of St. John's College, Cambridge. He matriculated in the Michaelmas Term of 1789 as a scholar. He was readmitted to the College as a Fellow-Commoner on April 17, 1794, took his M.B. in the same year and proceeded to M.D. in 1804. In 1795 he was appointed physician to the Army and in this capacity served in the Windward Islands, in Portugal, the Mediterranean, Egypt, &c. Returning to England he settled in London, was admitted a Candidate of the Royal College of Physicians April 8, 1805, and a Fellow on March 31, 1806. He delivered the Goulstonian Lectures in 1806-7, choosing the subject of yellow fever. He was Censor in 1808 and was elected physician to St. George's Hospital in that year. According to Munk, his health required a warmer climate, and he resigned his hospital appointment in 1811, going out to Jamaica as physician to the Forces. He died there on September 18, 1842, aged 70, being then deputy inspector of Army hospitals. He was buried in the yard of the Parish Church of Kingston, and is commemorated on a mural tablet erected by the physicians and surgeons of Jamaica, in the cathedral church.

Dr. John Haygarth, F.R.S., noted that Dr. E. N. Bancroft in 1809 made observations on 99 cases of typhus fever and inferred that the latent period of typhus varied from the thirteenth to the sixty-eighth day.

Dr. E. N. Bancroft inherited many of his father's characteristics and interests. He vigorously engaged in controversy, publishing in 1808 "A Letter to the Commissioners of Military Enquiry Containing Animadversions on the Fifth Report" and "A Refutation of various Misrepresentations published by Dr. McGregor and Dr. Jackson in their Letters to the Commissioners of Military Inquiry".

He expanded his Goulstonian Lectures into *An Essay on the Disease Called Yellow Fever, with Observations Concerning Febrile Contagion, Typhus Fever, Dysentery and the Plague*, 8vo, London, 1811. This work, as already mentioned, was edited by his father. He followed this up by *A Sequel to an Essay on the Yellow Fever, Principally Intended to Prove by Incontestable Facts and Important Documents that the Fever called Bulam, or Pestilential, has no Existence as a Distinct or a Contagious Disease*, 8vo, London, 1817.

These books contain many interesting records of disease, but their value is unfortunately destroyed by the author's bias in favour of the theory of non-contagion and by his endorsement of a contemporary belief that yellow fever and malaria were identical.

Like his father, Edward Nathaniel was also a botanist and zoologist. He published papers in the *Zoological Journal*: (1) *On the Fish Known in Jamaica as the Sea-Devil* (1829); (2) *Remarks on Some Animals Sent from Jamaica* (1830); (3) *On Several Fishes of Jamaica* (1831); (4) *Account of Several Fishes and Other Animals of Jamaica* (1832-34) and two botanical papers: (a) *On the Medicinal Plant Called Cnichunchulli, Comparative Botanical Magazine* (1835); (b) *An Account of the Tree Which Produces the Hog-gum of Jamaica, Journal of Botany* (1842).

Samuel, another of Dr. Bancroft, Snr.'s sons, was born in 1775. Like his brother he was educated at Dr. Burney's School. At the age of 17 he matriculated at Trinity College, Cambridge, on May 25, 1792.

In addition to those I have already mentioned in the course of this paper, I should like here to express my thanks to Sir Henry Dale, President of the Royal Society, and Mr. J. D. Griffith Davies, Assistant Secretary, who have helped me with information about Bancroft's Fellowship and communications to the Royal Society. Mr. Johnston Abraham and the Secretary of the Medical Society of London have informed me about Bancroft's membership of the Society.

On Bancroft's work on dyes I have been helped by Mr. C. Bolton and Mr. Lawrence Morris, the Editor of *The Dyer*.

CONCLUSION

The elder Bancroft is one of the most complex personalities in medical history. He was a genius endowed with great natural gifts, and coming as an unknown person to this country early achieved a distinguished position as a scientific physician and chemist. He soon had many influential friends—he had an attractive, hospitable, and kindly disposition—and he made the most of every opportunity that came his way. He was a pioneer in applied chemistry and learned in zoology and botany. In these fields he had an international reputation, and mankind is indebted to him for his work. He had a facile pen and his scientific and political writings are able and informative. He had, indeed, a fatal gift of versatility, which has proved a snare for his posthumous reputation. Some American historians stigmatize him as a scoundrel and a glaring example of perfidy. Dr. Wharton,⁴ contesting George Bancroft's attack on Bancroft before the

⁴ DR. WHARTON: *Revolutionary Diplomatic Correspondence of the United States*, I, 640-641.

The captives were kept confined during ten hours and when at six in the morning the door was opened, it took twenty minutes to clear away the bodies that were piled up against it. The dead were thrown into a ditch and the twenty-three still living were allowed to lie on the lawn in front of the Fort. Among the survivors was a Mrs. Carey, the Eurasian wife of a naval officer, who had perished in the "Black Hole"; the widow later married a military officer and lived in Calcutta till 1801. According to her statement, her mother and a sister, a girl of ten years, had been in the "Black Hole" and had perished with some wives of soldiers.

The tragedy of the "Black Hole" deeply stirred public opinion in Great Britain. In 1757 an expedition under Rear-Admiral Charles Watson (1714-57) and Lieut.-Col. Robert Clive (1725-74) regained possession of Calcutta. The Siraj-ud-Dowlah was defeated at the battle of Plassey, on June 23, 1757; he fled, but was captured on July 4, 1757, and put to death by native conspirators headed by Mirán, son of Jafar.

When all the circumstances are considered, it may seem strange that so many could die from the lack of oxygen or breathing air. The floor space was 308 square feet, which gave scanty standing room; the corresponding breathing space must have been about 30 to 40 cubic feet per person; it is true that the expired moisture, settling in still air, would soon render the atmosphere unbearable. The night was said to have been particularly hot and close; it was the rainy season and the wet bulb temperature may well have been in the neighbourhood of 34° Centigrade.

Had the prisoners kept perfectly still, more would have survived; but the unfortunate people crushed against the door in a vain attempt to burst it open and then tried to crowd to the windows for a breath of relatively fresh air.

Then there is this to be considered; it has been ascertained that if human beings are closely confined in a room, the walls of which are near or above body-heat, so that little or no vital warmth can be absorbed, the temperature of the bodies will rise approximately by 1° C. per hour. Once fever heat is reached, delirious conditions will follow, with convulsions, coma and death. This death by heat-stroke may not be a common occurrence, because the walls are usually sufficiently cool to reduce the heat and condense steam; but in the "Black Hole" of Calcutta several adverse circumstances prevailed.

It can be gathered from Holwell's report that many deaths occurred soon and since the dead would not consume oxygen or help to increase the temperature, the several adverse factors that have been mentioned must have contributed to kill many. Those that survived seem to have been near the barred windows, where they could stand upright by holding on to the bars and breathe untainted air. It can be surmised that many were simply stifled by pressure on the ribs, paralysing lung and cardiac action and thus stopping respiration; this would occur among those pushing against the door, whose bodies took over twenty minutes to remove. Many others within the guardroom may well have succumbed to heat-stroke.

BRIEF BIOGRAPHICAL NOTES ON J. Z. HOLWELL

John Zephaniah Holwell was born in Dublin, September 17, 1711, the son of Zephaniah Holwell (d. 1729), a timber merchant and son of John Holwell (1649-86), astrologer and mathematician. John Zephaniah went to school in Richmond, Surrey, and then began a commercial career in Holland. He soon returned to London, was articled to a surgeon in Southwark and attended Guy's Hospital for further instruction, under the Senior Surgeon, Andrew Cooper. In 1732 Holwell became a surgeon's mate on board an Indiaman bound for Calcutta: after a few voyages he obtained an appointment on shore, was granted the rank of a "Surgeon-Major" and settled in Calcutta in 1736. After a period of leave at home, he returned to India in 1751 as a "covenanted civilian".

Having survived the night in the "Black Hole" he was conveyed as prisoner with three others to Murshibad, in a very bad state of health and covered with boils. Holwell was eventually released on July 17, 1756, on the intercession of the Begum of Bengal, who, it is said, recognized his services to ailing Indians. Holwell then returned to England on the sloop "Syren" in February 1757; the voyage took five months, during which time he wrote an account of the events in the "Black Hole". He returned to Calcutta in 1759 and was appointed Governor in 1760, but disagreeing with the Board of Directors in the September of the same year he resigned; thereupon Mr. Henry Vansittart succeeded as Governor. Holwell then went back to England, lived in retirement at Pinner near Harrow, where he died on November 5, 1798. He was twice married; one son and two daughters survived him. His house still exists in Pinner.

According to unbiased reports Holwell was a capable administrator and a keen student of Oriental customs and languages, about which he wrote several essays; these were

with incompetence and dismissed. The command of the station was left to a surgeon, John Zephaniah Holwell, who enrolled as militia the remaining Europeans; they fought till their ammunition was exhausted and then surrendered, the Nawab assuring Holwell that they would be honorably treated. According to most accounts 146 were captured, with only one woman among them, but other records indicate that possibly there were four or five.

Holwell reported that 146 persons were thrust into the guardroom of Fort William at eight o'clock on Sunday evening, June 20, 1756. The building was demolished in 1818, so that no exact figures are available as to the size of the "Black Hole", but most authors concur in saying it was 22 feet in length, by 14-15 wide; height is quite uncertain, but Holwell considered it a cube of 18 feet a side. There were two small barred windows on the west side; from illustrations one surmises that the height inside could not have been above 12 feet.



Portrait of J. Z. Holwell by Sir Joshua Reynolds. (From *Echoes from Old Calcutta*, by H. E. Busteed, 2nd Edition, 1888, published by Thacker, Spink & Co., Calcutta.)

Holwell's account of the night is terrifying, even though it is moderate in tone and matter-of-fact in assertions. The wretched prisoners crowded against the door in a vain effort to burst it open; those at the windows made desperate attempts to bribe the guards outside or to purchase water for fabulous sums. Very soon the atmosphere became stifling, thirst unbearable; Holwell confessed having attempted to drink his urine, but its sharp taste made him desist. He appears to have been at one of the windows most of the time since he tried to parley with the guards; but none the less the perspiration from his body was so profuse that a fellow prisoner was able to allay thirst from his shirt-sleeves. Others stripped off their clothing and soon sank to the floor lifeless.

Section of Pathology

President—Professor W. G. BARNARD

[October 17, 1944]

Pathology

PRESIDENT'S ADDRESS

By W. G. BARNARD, F.R.C.P.

I would write,
Not of what Beauty and Truth may mean, but what concerns us more,
How knowing what they are, we best for our own ends may use them.
"Windfalls" by R. C. Trevelyan.

It appears likely that the time will soon come for reconstructive action and the flood of reconstructive proposals will recede. We in Pathology cannot and we would not wish to escape inclusion in this burst of reformatory zeal and because of this I think it profitable to consider the road pathology has so far travelled, its present position and to speculate as to its future progress.

Pathology is the study of disease processes, their cause, how they start, how they progress, their termination and how the body reacts and adapts itself to damage or injury.

The immediate interest of the physician is the patient, the immediate interest of the pathologist is the disease. These interests are not in conflict, they are complementary.

Pathology is of course a part of Medicine but if by some magic medicine and surgery should cease, pathology could still go on. It is a science in its own right and its achievements have warranted its independent existence and the pursuit of its own end which is the study of pathology. As it has grown it has developed along different lines so that it appears as a curious mixture of bacteriology, chemistry, experimental pathology, morbid anatomy and morbid histology. Some of these parts growing up with pathology have shot out branches which have no direct bearing on pathology although highly important to themselves.

Being a part of medicine the history of pathology can be traced to the earliest times. It is an instructive and in some respects an amusing research to find how far back ideas on disease processes can be traced. Some not only find pleasure in such delving but in the light of modern knowledge try to attribute to some chance remark or speculation a meaning which could not have been intended at the time it was made.

But pathology as we understand it to-day is surprisingly young.

The first independent pathological society, the New York Pathological Society, has reached its centenary this year and our own society, the London Pathological Society, which is the next oldest, is only ninety-eight years old. If we turn to journals, the first largely pathological was *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* started in 1847.

The first Chair of Pathology in this country was established by the London University in 1827 when J. F. Meckel was appointed Professor of Morbid and Comparative Anatomy but he did not take up his duties. In 1828 Sir Robert Carswell was nominated to, but did not occupy, the Chair until 1831. At Cambridge the Chair of Pathology was established by Grace on December 6, 1883, and the first Professor appointed 1884. In the Dreschfeld Memorial volume published by the Manchester University Press 1908 it is claimed that the Chair of Pathology at Owens College to which Dreschfeld was appointed in 1882 was the first Chair of Pathology in this country.

If we turn from Societies, Journals and Chairs to people we will find that there is an overlap between some of the founders of our science and some of our still active members. To illustrate this I have prepared a chart showing some at any rate of those who will be accepted as founders of modern pathology. The chart has no claim to be in any

printed and obtained the approbation of Voltaire who wrote: "Nous saisissons avec reconnaissance cette occasion pour rendre ce que nous devons à cet homme, qui n'a voyagé que pour s'instruire." Holwell was the author of some polemical pamphlets which explained his differences with the Board of Governors of the East India Company. Apart from *A genuine narrative of the deplorable deaths, &c.* (London, 1758), only one medical work is known from his pen—an essay with the comprehensive title:

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CONCLUSIONS

The deaths in the "Black Hole" of Calcutta have been often quoted as an example of the dangers resulting from deficient aeration in closed spaces, for it was thought that the casualties were due to an excess of vitiated air or CO₂, or perhaps to a lack of oxygen. Actual tests and experiments have not confirmed such an explanation.

There have since been several similar accidents, which were also considered to have been caused by impure or vitiated air; for example, when 500 Austrian prisoners were shut up in a room after the battle of Austerlitz—December 2, 1805—and only 40 survived.

Then on December 2, 1848, in the steamer "Londonderry", plying between Sligo and Liverpool, 200 passengers were confined in a battened hold, 18 feet long, 11 feet wide and 7 feet high; on this occasion 72 died. It was noticed that the victims were bleeding from the nose, ear and even eyes; presumably there was some contributory cause; perhaps fumes from the boiler-furnaces, with CO?

Reverting to the deaths in the "Black Hole" it seems as if the casualties in the first half-hour or so must have been due to suffocation through crushing; recent events have shown how easily people can be crushed and suffocated by weight, without there being any lack of air. In Calcutta, heat-stroke provided a sufficient reason for many becoming delirious and then dying. According to this interpretation, heat-stroke would be due to a combination of a hindered perspiration through excessive humidity in the air and increasing heat in the air of the room because the walls were not condensing the steam or water-vapour.

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Section of Pathology

President—Professor W. G. BARNARD

[October 17, 1944]

Pathology

PRESIDENT'S ADDRESS

By W. G. BARNARD, F.R.C.P.

I would write,
Not of what Beauty and Truth may mean, but what concerns us more,
How knowing what they are, we best for our own ends may use them,
"Windfalls" by R. C. Trevelyan.

It appears likely that the time will soon come for reconstructive action and the flood of reconstructive proposals will recede. We in Pathology cannot and we would not wish to escape inclusion in this burst of reformatory zeal and because of this I think it profitable to consider the road pathology has so far travelled, its present position and to speculate as to its future progress.

Pathology is the study of disease processes, their cause, how they start, how they progress, their termination and how the body reacts and adapts itself to damage or injury.

The immediate interest of the physician is the patient, the immediate interest of the pathologist is the disease. These interests are not in conflict, they are complementary.

Pathology is of course a part of Medicine but if by some magic medicine and surgery should cease, pathology could still go on. It is a science in its own right and its achievements have warranted its independent existence and the pursuit of its own end which is the study of pathology. As it has grown it has developed along different lines so that it appears as a curious mixture of bacteriology, chemistry, experimental pathology, morbid anatomy and morbid histology. Some of these parts growing up with pathology have shot out branches which have no direct bearing on pathology although highly important to themselves.

Being a part of medicine the history of pathology can be traced to the earliest times. It is an instructive and in some respects an amusing research to find how far back ideas on disease processes can be traced. Some not only find pleasure in such delving but in the light of modern knowledge try to attribute to some chance remark or speculation a meaning which could not have been intended at the time it was made.

But pathology as we understand it to-day is surprisingly young.

The first independent pathological society, the New York Pathological Society, has reached its centenary this year and our own society, the London Pathological Society, which is the next oldest, is only ninety-eight years old. If we turn to journals, the first largely pathological was *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* started in 1847.

The first Chair of Pathology in this country was established by the London University in 1827 when J. F. Meckel was appointed Professor of Morbid and Comparative Anatomy but he did not take up his duties. In 1828 Sir Robert Carswell was nominated to, but did not occupy, the Chair until 1831. At Cambridge the Chair of Pathology was established by Grace on December 6, 1883, and the first Professor appointed 1884. In the Dreschfeld Memorial volume published by the Manchester University Press 1908 it is claimed that the Chair of Pathology at Owens College to which Dreschfeld was appointed in 1882 was the first Chair of Pathology in this country.

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The Twort d'Herelle phenomenon, bacteriophage and viruses have opened new flood-gates of activity. Bacteriology has progressed by the identification and description of an ever-increasing number of new organisms, by investigating the reactions they produce in man and other animals, and in addition, in more recent times, in examining the physiology of the bacteria themselves and in the reaction the activities of one organism may have on the growth of another.

Biochemistry.—The major contributions of biochemistry to pathology are of even more recent date than those of bacteriology. I am well aware of the interest taken in the science by physicians of long ago. For instance, if we turn to art we will find that in pictures of the seventeenth century dealing with medicine it was usual to allow a prominent place to the examination of urine. This was especially true of the Dutch School and there is a particularly attractive picture of the kind by Gerard Dow in Buckingham Palace. Such examination was even used in the diagnosis of chastity and pregnancy. However, according to Garrod, alcaptonuria, black urine, was first observed by G. A. Scribonius in 1609. Albuminuria was first detected in 1694. Wohler working with Liebig effected in artificial synthesis of urea in 1828. From this time onwards chemistry concerned with fermentations, digestion, metabolism, hormones, internal secretions and the composition and reactions of the body fluids has contributed much to pathology.

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Modern morbid anatomy and histology spring from the time when the naked-eye findings could be checked by the microscope and other means. Considering the lack of these means the accuracy of the records left by the great pathologists of the earlier time is surprising.

The cellular theory of Virchow marked the beginning of modern morbid anatomy and histology. Interesting as it might be we have not time at our disposal to trace the steps through Robert Hooke, Robert Brown, Valetin, Schwann and Mohl which led to the formulation of this famous theory. I will content myself by quoting Boas who says: "The cellular theory like all theories is to be regarded as a historical expression of the scientific tendency of a certain period." This does not in the least detract from the significance of the theory nor from the distinction accorded to Virchow for formulating it.

As has already been said, modern morbid anatomy and histology probably owes most to Virchow but it also owes almost as much to Cohnheim and Kölliker. Its progress has been largely that of sorting out, classifying and describing lesions in the body. Most of the advances have been associated with improved histological technique. The progress has been slow but sure.

Experimental pathology.—During its earlier days most pathologists began their careers in morbid anatomy and histology. If they extended their activities to bacteriology or biochemistry or experimental pathology they looked for a new label to describe their activity. In a similar way the label "experimental pathology" was adopted by those workers chiefly engaged in experiments.

The title is a little misleading because all pathologists should be experimental pathologists but there are some who are more attracted to and have a special gift for experimentation. With some diffidence I would suggest that morbid anatomists have not used experimental methods as much as they should. It is a method which particularly lends

way exhaustive. It is only intended as a visual indication of the period of activity of a few who contributed to the development of modern pathology.

	1850	1855	1860	1865	1870	1875	1880	1885	1890	1895	1900	1905	1910	1915	1920	1925	1930
PASTEUR																	
KOCH																	
COHN																	
KLEBS																	
EHRlich																	
WELCH																	
THEOBALD SMITH																	
ALMROTH WRIGHT																	
LIEBIG																	
WOHLER																	
EMIL FISCHER																	
GOWLAND HOPKINS																	
HALDANE																	
FOLIN																	
CLAUDE BERNARD																	
METCHNIKOFF																	
HENLE																	
KÖLLIKER																	
VIRCHOW																	
COHNHEIM																	
SHATTOCK																	

The chart calls for few comments, the first group were responsible for the development of bacteriology, the second for chemical pathology and the third for morbid anatomy and histology. Here are a few incidents which illustrate various aspects of my theme. In 1876 Koch reported to Cohn that he had worked out the complete life-history of the anthrax bacillus. Cohn invited Koch to his laboratory and there he gave a three-day demonstration of his discovery in the presence of Cohn, Weigert, Cohnheim, Auerbach and Traube, an unusual assembly before which to demonstrate a principle of bacteriology. Here in London at King's College at the International Medical Congress in 1881 Koch demonstrated the growth of bacteria in pure culture on solid media, a proceeding fundamental to the development of bacteriology. It is, I suggest, a pertinent comment to make of medical opinion of that time that there is no reference to this demonstration in the official index of the Congress, nor does Koch's name appear in the list of authors. The only reference that I have been able to find to the demonstration appears in "Joseph Lister's" opening to a discussion "On the Relations of Minute Organisms to Unhealthy Processes Arising in Wounds, and to Inflammation in General". Bulloch says that in addition to Lister, Pasteur, Sanderson and Chauveau were present at the demonstration. Although this demonstration is not recorded, Dr. Bastian's reiteration of his views on spontaneous generation is duly recorded.

Paul Ehrlich was a friend of Sir Almroth Wright and so forms one of the close links with our time. Liebig wrote the first book of its kind entitled "Organic Chemistry in its application to Physiology and Pathology". Emil Fischer has been described as "the pathfinder of carbohydrate chemistry" and was also concerned with the isolation of amino-acids and the investigation of enzymes. Henle wrote a "Handbook of Rational Pathology" and a monograph on Urinary Casts. Kölliker was famous as the author of a "Handbook on Human Histology" and also as a master of comparative histology.

It will be clearer if something is said about the way in which the parts of pathology have developed rather than dealing with them altogether.

Bacteriology.—Bacteria were guessed at by Fracastoro and some one hundred years later were seen and illustrated by Leeuwenhoek (1683). But the real fathers of modern bacteriology were Pasteur, Cohn and Koch. Cohn is perhaps not quite so well known as the other two but Bulloch has pointed out that: "The whole modern superstructure of bacteriology has been erected on Cohn's conception that bacteria show consistency of form and specific differences among each other."

Ferdinand Cohn was Professor of Botany at Breslau, Pasteur was a chemist and Koch a doctor of medicine so that the foundations of bacteriology were laid by a botanist, a chemist and a doctor.

It may be remarked in passing that this affords an exceptionally good example of the way in which pathology has developed. It adds to its knowledge material gleaned from sources which do not at first appear to be directly connected with it. From the beginning bacteriology has shown two distinct though often mingled trends, one is exemplified by Pasteur who was chiefly concerned with infectious disease, how produced and recovered from, and the other by Cohn and Koch who studied bacteria, their cultivation and characters. Since their day bacteriology has grown not only as an essential part of pathology but has extended far beyond into a wide world of minute organisms most of

which are not pathogenic to man. Bacteriology is so firmly established that even the general public is becoming increasingly bacteria-conscious. Much of the progress has been linked with new methods of investigation, cotton-wool, solid media, Petri dishes, staining methods and improved microscopes. During the same period the work in immunity has been prodigious both in the amount of work done and in the literature it has evoked. The injecting needle has become an essential armament of war and doubtless will play an ever more active part in peace. From the cradle to the grave our relations to bacteria will be public as well as personal and private concerns.

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itself to the testing of ideas and may well give an answer in a very much shorter time than that taken to accumulate surgical or post-mortem material. The newer branches, bacteriology and biochemistry, have made good use of experimentation.

In experimental pathology there is clearly an overlap between physiology and pathology. Before he can recognize the abnormal the pathologist must have a working knowledge of the normal. The abnormal will often shed light on the normal both as far as function and structure are concerned. For these reasons and from the earliest times physiologists have been interested in the abnormal and pathologists in the normal. The earliest master of the experimental method was Harvey. Probably the more immediate father of this method was Claude Bernard, not only for his devotion to experiment but perhaps even more for his critical attitude to his own work. He held the view that the chief aim of physiological experimentation was to throw light upon morbid conditions and in 1872 he gave a course of lectures on experimental pathology. Physiologists and biochemists have maintained this interest in morbid conditions and have contributed much to their understanding. Pathology has also contributed much to physiology. To give one small example, probably the greater part of the earlier knowledge of the ductless glands came from pathology. All knowledge of abnormal function as well as of structure is a part of pathology and contributions to this knowledge are welcome whether they are made under the guise of physiology or any other science. The primary object of the physiologist is the study of the normal, that of the pathologist the morbid. The pathologist welcomes the invasion of his territory by any who care to work in it but the difference in outlook will colour the interpretation of the different workers. And I would insist that there is a difference in outlook between physiology and pathology. Lest I should be accused of splitting hairs I would quote Halliburton's opinion when discussing physiological or functional albuminuria. He says: "I always feel inclined to object to the adjective physiological, for one must regard the condition under which it occurs as being really pathological even though the morbid condition is not a very serious one."

I might not have mentioned the matter but for a suggestion that has been made that physiologists might teach some part of pathology. That I believe would be a retrograde step.

Experimental pathology has to its credit the vast enterprise associated with cancer research. I suppose there is no subject about which we know more largely due to this enormous activity and yet fail to know that part which would be of the greatest interest to medicine and to the patient.

Clinical pathology.—So far I have said nothing about clinical pathology. I believe it to be an essential part of pathology. There are some who would separate it from pathology and some who would welcome its absorption by medicine. It suffers from having a utilitarian side which is overwhelmingly obvious and that is at once its chief danger. At its best it should be a firm link between clinical medicine, bacteriology, chemical pathology, morbid anatomy and histology, haematology and any of the other divisions into which pathology may be separated. At its worst it is a penny-in-the-slot machine in which specimens arrive at one end and reports fall out at the other. Its usefulness is so well understood that even politicians and the lay public demand its application in the practice of medicine. Indeed I feel that because of this popularity and because of this demand it is in grave danger of becoming segregated and separated from pathology and then it might deserve some of the less complimentary remarks which have been made about it. For its own sake I think we should strive to keep a firm bond between it and the more academic sides of pathology. And I think those of us who are in academic pathology should do all we can to devise means by which this bond shall be strengthened and maintained. The thought of countless scattered, isolated, purely utilitarian laboratories distributed all over this country under any new scheme appals me. And if it comes about it will be a bad thing for pathology as well as for clinical pathology.

Present position.—I have indicated in brief outline part of the path along which pathology has so far passed. I need not say much about its present state as I am addressing pathologists, to discuss it at length would not only be unnecessary, it might even be impertinent.

We might, however, consider the general pattern of our activities and reconsider our aims. It appears to me in general that we are all following the traditional lines that I have traced. There has been great progress and in our own time phage and viruses have been added to the mass of micro-organisms which have been further sorted out. There are indications of greater interest in bacteria for their own sake, their physiology, structure, methods of division and the like. The study of their action in the body and the body's reactions to them is still being actively pursued. Penicillin is a triumph of scientific vision and handling of what was at first an accidental and unwelcome incident. It may well prove to be the major contribution of our time. The activities of biochemistry are

extending and its ever-growing interest in bacteriostatic substances, metabolism, vitamins, internal secretions and the body and tissue fluids promise to increase our understanding of function and reactions of the body. Morbid anatomy and histology continues its solid, slow advance; unspectacular perhaps but an advance none the less real though its fanfares are few. Pathology is an integral part of medicine, and its contribution has been great and is ever becoming greater. In Bernard's time, following an exposition of his experimental findings, a Paris physician remarked that Physiology was a science de luxe which could well be dispensed with in practical medicine. In the past a somewhat similar attitude has been taken towards pathology but this has now largely disappeared. There is to-day a better understanding between the clinician and the pathologist than ever before. We appreciate, and it would be impossible to exaggerate, the contributions that clinicians have made to pathology. And in clinical science, largely sponsored by Sir Thomas Lewis, clinicians are likely to add still more to pathological knowledge. Sir Thomas, writing of clinical science, says: "In the centre of this field is the human patient, and here the work is upon the living man, but relevant to this clinical work is that of the remaining great departments of pathology—namely, experimental medicine, morbid anatomy, clinical pathology, pathological biochemistry, and bacteriology. Strictly speaking, there is between clinical science and human pathology, using each of these terms in the broadest sense, no difference."

This new bond between clinician and pathologist and the new emphasis on the study of the pathology of the patient augur well for new advances in our science.

The field is wide and expanding: the activity is great and continuing: the integration is difficult and largely lacking. At this stage in our history this lag is I suppose inevitable. A little earlier pathologists were growing up with the growing and developing branches of pathology. I propose to illustrate this point by reference to one of my earlier teachers. Professor Bulloch was generally regarded as a bacteriologist, a very distinguished bacteriologist. And yet the first course in general pathology I attended was given by Professor Bulloch. He was a pathologist who had grown up with the growth of bacteriology and although adorning a Chair of Bacteriology was still a pathologist. There are few left to-day who have grown in a similar manner and as a result the separation of pathology into its several parts is now more noticeable than its unity.

The future.—Since the future is known to none of us I feel a little less diffident in saying something about the future development of pathology. There will still be, as in fact there must be, separate avenues along which pathology will advance. Bacteriology would still be a science in its own right even if there were no pathology. So of course would biochemistry and the same could be said for cytology, and I expect that the divisions will increase in number rather than diminish. I see no indication of exhaustion in the advance. I do, however, see increased difficulty in maintaining the relation of the parts to the whole. There has been a continual budding off from medicine. Chemistry nurtured in our medical schools largely because of its pharmaceutical importance has now developed and evolved its own separate existence. Physiology has within our time staked its own claim to independence. And now pathology as a whole and its integral parts have become grown up and demand their own latch-keys. Such disruption in medicine is inevitable but it carries with it grave dangers detrimental to medicine as a whole. This is also true of pathology. It is easier to split than to fuse, and yet it is the task of pathology to extract from all sources all that will contribute to the understanding of disease processes and bodily adaptation and adjustment to injury.

So far in all the fields of Pathology our greatest activities have been in collecting data; adding to the known number of organisms describing them, their actions in and the responses they excite in the body; finding out the chemical nature of various fluids and substances, describing their acceleration and inhibition of various reactions; collecting and describing in ever greater detail diseased organs and tissues. We are in danger of burial beneath the accumulation of our own industry.

The first stage in the development of Science is usually the accumulation of facts; this forms an essential step but the second step is equally important and that is to use these facts upon which to build theories, generalizations, eventually laws.

As Arthur Thomson wrote: "As long as the collection and registration of facts pre-occupies the energies and attention, scientific enquiry has hardly begun."

It is not suggested that energies and zeal in accumulation should be discouraged but the time has come when greater effort, thought and encouragement should be given to the next phase in the progress of the development of pathology. It is of course a more difficult phase and one from which many of us shrink. One of the reasons for this shrinking is that there is a wellnigh universal fear that if a generalization is made or a law suggested it might be subsequently shown to be wrong and to have obscured truth

instead of revealing it. Bacon's historic aphorism declares: "Truth to emerge sooner from error than from confusion." And I suggest that the danger of hiding truth behind a false generalization is over-emphasized.

Generalizations or hypotheses are guesses at truth and should not end work but stimulate new work designed to test their validity.

All these different activities that we have discussed are brought together in pathology. It is this unity in pathology that must be maintained and to which we must give greater attention. All parts must contribute to this end. There is no aristocracy in science. Because we work in laboratories, or with defined chemicals or by experimental methods or that we do no "routine", or even that we have had great success, no one of these things makes one particular part superior to another. There is all too often as much routine work in a laboratory as there is in the wards or the post-mortem room, and work carried out in a scientific spirit in these places is as truly scientific as work done in laboratories. All parts have an equal obligation to contribute all they can to the whole and in order to do this the different parts must try to understand the aims and even the limitations of the other parts. There will be no simple solution to the problem. Among the recommendations of the Goodenough Committee is one suggesting that in the medical schools bacteriology, chemical pathology, clinical pathology and morbid anatomy be all grouped into one pathology department. This may help.

The different branches have become so great and will become so much greater that no man will be able to be master of them all. So that for this reason and also for their own good I suggest that in future each part of pathology should lay most stress on general principles. If this is done I believe there will be a better understanding of pathology.

Most of us are engaged in teaching medical students. It is clear that there will be less rather than more time for pathology in the curriculum of the general practitioner course. If this is so what should be our aim? I believe that if students can absorb the general principles of pathology, that is the principles of bacteriology and immunity, of chemical pathology and of morbid anatomy and histology, they will have acquired a sure foundation on which to build medicine and special pathology. If they do not get this grounding and instead get a haphazard collection of incidental but unrelated facts about diseases they will have no foundation for their future building.

Pathology is a science and, to quote Karl Pearson, the scientific method is marked by the following features: (a) Careful and accurate classification of facts and observation of their correlation and sequence; (b) the discovery of scientific laws by aid of the creative imagination; and (c) self-criticism and the final touchstone of equal validity for all normally constituted minds.

Clerk-Maxwell used to ask: "What is the go of this?" and when put off with some verbalism, persisted with: "What is the particular go of this?" The particular go of pathology in the widest sense is to discover the laws governing the reactions of bodies to injury. Some of the paths pursued may appear abstruse and unrelated to the immediate object. I mention this because one of the legitimate and probably fruitful lines of advance in the future will be organized research. I believe that there are many problems which should be attacked by such a method. I also believe whole-heartedly in the closest possible association of different research institutes and different university departments.

Let us not, however, rely overmuch on organization; let us always ensure that the man with a particular urge for a particular inquiry should always have his chance. Setting the problem and attacking it from all sides may well be a feature of our future progress. I would however like to remind you of part of his introduction to science written by Dr. Alex. Hill in 1900. He says: "Great advances have been made by investigators whose object was wholly technical. Yet, if the history of science were written, it would be found that the first step in advance, the germ of the discovery which became fruitful in the hands of the practical chemist, the mechanician, the pathologist, was discovered by the investigator, for whom science lost its interest as soon as it could be put to practical use."

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Section of Urology

President—F. MCG. LOUGHNANE, F.R.C.S.

[October 26, 1944]

Genital Tuberculosis

PRESIDENT'S ADDRESS

By F. MCG. LOUGHNANE, F.R.C.S.

GENITAL tuberculosis is never a primary infection, but is always secondary to a distal focus. The tubercle bacillus usually gains entry to the body either by the respiratory or alimentary system, and rarely through a cutaneous lesion. Pulmonary tuberculosis, active or latent, is generally present, because genital tuberculosis is always an infection by the human type of tubercle bacillus. A distinction should be made between the terms genital, genito-urinary, and uro-genital. In the literature these are often used indiscriminately or as though they were synonymous. Genito-urinary signifies that the urinary infection is secondary to the genital, and uro-genital that the urine is first infective. Genital tuberculosis can only be so described when no demonstrable tuberculous lesion can be found in the bladder and kidneys. The presence of tubercle bacilli in the urine does not necessarily mean an infection of the renal tract, unless the urine has been collected through a catheter. Even then, tubercle bacilli in the urine may be due to a prostatic tuberculosis, and this being so the findings of a catheter specimen may be equivocal, for the bacilli may be carried by the catheter from the infective prostatic urethra into a non-infective bladder. Prostatic tuberculosis, however, except as a secondary condition, is so rare that for practical purposes if tubercle bacilli are found in the urine then a renal lesion may generally be inferred.

STATISTICS

Genito-urinary tuberculosis is not a common disease. In the annual report of the London County Council for 1937, the total number of patients admitted to their 30 general hospitals was 202,485, of which 8,500, or 4.2%, were genito-urinary cases. These, however, included both male and female, and medical as well as surgical. Out of a total of 5,624 cases of tuberculosis genito-urinary cases numbered 97, i.e. 1.7% of the total general admissions, and 1.7% of the total admissions for tuberculosis. These figures are also inclusive of male and female, and medical as well as surgical.

These figures differ widely from American and continental records, where, apart from the greater population, there seems to be an increased incidence of tuberculosis. An average from several writers gives about 2% genito-urinary tuberculosis in all autopsies, and 12% in autopsies on tuberculous patients. These findings are terminal, however, and relate to the dead. I have been unable to find comparable figures in the living, such as those given in the London County Council report.

It is still disputed whether tuberculosis can be primary in the genital tract, or is always secondary to a renal infection. Wells maintains that a tuberculous epididymitis is a certain sign of renal tuberculosis. He bases his argument on an analysis of 55 cases of epididymitis, 30 of which ultimately developed frank renal disease, and 6 remained purely genital. In only 14 cases, however, were tubercle bacilli found in the urine at the time epididymitis was first diagnosed, while in 4 other cases tubercle bacilli were found only after a lapse of two years. In 5 cases renal tuberculosis was diagnosed

before epididymitis, in 13 cases a considerable time after, and in 13 cases both were diagnosed together. It is incorrect, therefore, from these figures, to infer that tuberculous epididymitis is always of renal origin. Established tuberculosis in either the renal or genital tract is apt to spread rapidly, and from one tract to the other, and that both will be involved at some time during the course of the disease is not surprising. In a series of 222 cases Young found the seminal vesicle involved alone in 47, the epididymis alone in 37, both together in 100, and an associated kidney lesion in 122. In another series of 336 genito-urinary cases Young found 108 were genital with no kidney involvement, and 71 were renal with no genital involvement. Kretschmer, in 94 cases of tuberculous epididymitis, found tubercle bacilli in the urine in 13, and a renal lesion in 10. It is evident, therefore, that an antecedent renal lesion is not always present. Statistics are interesting, but not conclusive, and they can be made to support almost any theory. In practice, however, one's own statistics are the most influential, however small these may be.

From a study of a large number of contradictory figures I am confirmed in my belief that it is impossible to be didactic and state categorically that genital tuberculosis is always secondary to kidney disease. It may be in many cases, but it cannot be proven in all, and there is no evidence that it should be accepted as the routine route of infection. Genital and renal tuberculosis may be discovered at the same time, and there is nothing to indicate which is primary and which secondary. The extent of a lesion is not necessarily an indication of its duration or priority, as is well known in cases of carcinoma, e.g. a small growth in the gall bladder may have extensive secondaries and be easily missed. Also, as renal and genital tuberculosis are metastatic and secondary to infection in the lung, they might both have become infected at the same time. Multiple bone lesions are not unknown. Hammond, quoting J. Hutchinson who states that in lupus vulgaris multiple lesions arise at first, most of which clear up, leaving only one or two chronic and recurrent, suggests that in genito-urinary tuberculosis multiple lesions may also occur at the beginning, with later only one or two isolated sites of infection persisting. Band and others have shown that tuberculous bacilluria generally indicates a renal infection, and that many healed renal foci can be demonstrated microscopically, that probably both kidneys are infected at the beginning, that one overcomes the infection and remains healthy, although the other succumbs and must be removed. The possibility and probability of multiple infection must therefore be accepted.

INCIDENCE

Primary tuberculosis of the prostate is very rare. Keyes found in 1,215 autopsies 343 cases of pulmonary tuberculosis, and in only one of these was the prostate alone involved. Barney could find in the literature only 5 authenticated cases of primary prostatic tuberculosis, and Young, in his extensive experience, had only one personal case. Hammond reported one case of primary infection, and in French literature I have come across 4 cases. K. Walker in 1911 reported 3 cases, and Saxforth in 1910 found 9 cases in 10,016 autopsies. It is not mentioned, however, whether other tuberculous lesions were present, and if they were, how a diagnosis of primary tuberculosis was arrived at.

Secondary infection, on the other hand, is very common, an average of many statistics being from 60 to 70% of cases of tuberculosis of the prostate. Personally I have only encountered 4 cases of prostatic involvement in a series of 13. Primary tuberculosis of the seminal vesicle also appears to be rare, though Young believes otherwise, but his reasoning is not convincing. There are no autopsy figures showing tuberculosis of the seminal vesicles alone, and there are no early symptoms to indicate a diagnosis. The facts that the globus minor of the epididymis is most commonly infected, and sometimes only a small nodule of tuberculosis may exist there while the vesicle is markedly involved, are the chief arguments in favour of primary vesiculitis. In the 55 cases of tuberculous epididymitis analysed by Wells, the vesicles were affected in 11 cases, not involved in 16, and in 28 there was no record. It has already been mentioned that the severity of a lesion is no indication of priority or time of infection. That a primary vesiculitis can occur none can deny, but that it has actually occurred has never been proved.

Secondary vesiculitis is more common than secondary prostatitis, and is reported in 80% of cases. If the primary kidney or epididymis, however, were earlier diagnosed and removed, these secondaries in the prostate and vesicles might be of rare occurrence.

The epididymis is the principal site of primary genital tuberculosis. According to Hammond, 30% of the patients when first seen have unilateral epididymitis, with no lesion in the prostate or vesicle, but if they are present then 25% are bilateral. Young's figures suggest that the vesicles are more commonly affected, being 47 out of 222 cases of genital tuberculosis, whereas the epididymis was alone infected in 37. It is difficult

to believe, however, that a clinical diagnosis of isolated vesiculitis can accurately be made, while it is common knowledge that isolated epididymitis is often found, and that a diagnosis of tuberculous vesiculitis or prostatitis is seldom made in the absence of epididymal or urinary infection. In 4,250 autopsies at the Boston City Hospital, there were 35 cases of tuberculous epididymitis. In 25 of these the vesicles and/or prostate were affected, but in 10 the epididymis alone. Of 80 cases in St. Thomas's Hospital reported by Lee, 40% were unilateral epididymitis alone, and 50% unilateral epididymitis with involvement of the prostate and vesicle.

Epididymitis secondary to a urinary infection is common. Of 342 cases of uro-genital tuberculosis Young found only 71 renal with no genital involvement.

Primary tuberculosis of the testis is unknown. It is always secondary to an epididymitis, and occurs, according to Barney, in 83% of cases within a year.

Tuberculosis of the urethra is rare, which is surprising seeing that for years tuberculous urine may be flowing along it. Trauma from rough instrumentation may incite an attack of urethritis.

Tuberculosis of the glans is also rare. There are only 25 cases in the literature, and 22 of these followed ritual circumcision in Jewish children. Though seldom due to coitus, Lazarus and Rosenthal reported one undoubted case, which was so persistent and widespread that eventually the penis had to be amputated. In French literature I have found one other case.

ROUTE OF INFECTION

The tubercle bacillus can reach the epididymis by the blood-stream, by lymphatic extension, or by the lumen of the vas.

In favour of hæmatogenous infection are the facts that in most cases when first seen the epididymis alone is infected, and that in many cases the urine is free from tubercle bacilli, and pyelography reveals no abnormality of the kidney. Wells thinks a blood-borne infection unlikely, because frequently both epididymides are involved consecutively, and he considers that both should be attacked via the blood-stream to be too striking a coincidence. He does not hesitate to assert, however, that renal tuberculosis is blood-borne and generally bilateral. Both Carver and Hammond believe in hæmatogenous infection. Young, however, says that the seminal vesicle is always involved first, and points out that the globus minor is generally attacked before the globus major. Primary infection of the globus major, however, is not infrequent, and in many cases when first seen it is impossible to say where the disease started. It is well known also that ligation of the vas prior to a prostatectomy does not always prevent epididymitis. In favour of ascending infection along the perivascular lymphatics are the presence of tuberculous nodules in the vas, the facts that both ends of the vas are extensively diseased and that infection of the seminal vesicles nearly always precedes bilateral epididymitis. Lymphatic extension of tuberculosis is a common occurrence in other parts of the body and there is no evidence to suggest that it does not happen in genital tuberculosis.

That infection should reach the epididymis through the lumen of the vas is not impossible, but highly improbable. How a non-motile bacillus can ascend against the stream in a very narrow channel, against peristalsis and against ciliated epithelium, is difficult to explain. The orifice of the ejaculatory duct is very minute, and a reflux from the prostatic urethra could only occur if the duct were diseased and gaping or the fluid in the prostatic urethra under great pressure. In the absence of vesiculitis urethroscopy never shows diseased duct orifices. An ascending infection up the lumen of the ureter has been shown experimentally not to occur, and reverse peristalsis can only happen if the lower ureter is obstructed. There is no reason to believe that the vas behaves differently. Also, after epididymectomy or division of the vas a urinary fistula is rare. It is quite true that very occasionally a drop of urine has been seen to emerge from the cut vas, and the theory that non-specific epididymitis is due to irritation caused by a little urine being forced up the vas into the epididymis is attractive and generally accepted. Non-specific epididymitis, however, is most prevalent amongst soldiers in training, and it is understandable that the combination of a full bladder and strenuous exercise might produce a reflux from the prostatic urethra. Moreover, in only 30% of patients, when first seen for epididymitis, are tubercle bacilli found in the urine.

SYMPTOMS

Acute tuberculous epididymitis occurs in about 5% of cases, and cannot at first be distinguished from *Bacillus coli* or gonococcal infection. The preceding history, however, will be helpful. The disease usually becomes chronic in a tuberculous infection, occasionally

so with *Bacillus coli* and frequently in the case of the gonococcus. When this does happen the specific characteristics become more pronounced. In tuberculosis the initial hydrocele disappears and the cavity of the tunica vaginalis becomes obliterated with adhesions. The rugosity of the skin of the scrotum becomes increased because of œdema and adhesion to the testis and epididymis. An abscess or discharging sinus is often present. The cord is thickened, also the vas, which may be nodular. On rectal examination one or both vesicles may be thickened and palpable, less often the prostate. A very early diagnosis is fraught with danger. McGavin, from St. Bart's Hospital figures, found that 30% of epididymides removed for tuberculosis were non-tubercular on microscopic examination. Yet if an early diagnosis is not made epididymectomy is a doubtful procedure, for extension to the testis and vesicles rapidly occurs. Barney reports 3 cases of doubtful tuberculous epididymitis where operation was delayed, and which later at operation were found to be sarcoma. He rightly says: "If in doubt operate", for it is better to remove a doubtful tuberculous epididymis or testis than to leave a sarcoma to mature.

Insidious onset and chronicity with progression are the chief characteristics of tuberculous epididymitis. The testis only becomes involved after the globus major, and usually at operation the condition is one of epididymo-orchitis, for an exploratory incision into the testis often reveals infection. In 83% of cases the testicle is said to become infected within a year.

Pain, tenderness, and fever are slight and insignificant.

There are no special symptoms of vesiculitis. The patient generally complains of an enlarged epididymis, and the diseased vesicle is only discovered on routine rectal examination.

In the beginning a tuberculous prostatitis is silent and devoid of symptoms, and is only discoverable on rectal examination. The disease is progressive, culminating in caseous degeneration, abscess and sinus formation. Calcification and fibrosis are uncommon. Symptoms of urethritis may develop, and tubercle bacilli will be found in the discharge. Sometimes the disease is only accidentally discovered after microscopy of an adenoma removed suprapubically. If there is frequency of micturition and tubercle bacilli are found in the urine, and there is no evidence of renal or other genital tuberculosis, then a primary tuberculous prostatitis may be inferred. Blanc, of Bordeaux, suggests the following technique to clinch the diagnosis: Irrigate the bladder with oxycyanide of mercury; then fill the bladder with sterile water; empty the bladder naturally and examine for tubercle bacilli. If none are found pass the remainder after prostatic massage, and if tubercle bacilli are now present the case is one of primary prostatic tuberculosis.

DIFFERENTIAL DIAGNOSIS

Acute primary epididymitis cannot be distinguished from that due to other organisms, and it has been known to occur during an attack of gonorrhœa. One must wait for the chronic phase before making a definite diagnosis, when gonorrhœa, syphilis, non-specific disease and tumours have to be excluded. Associated disease of the seminal vesicle is the surest indication that the epididymitis is tuberculous, but if diagnosis is to be withheld until this occurs, it might be advisable to do an Aschheim-Zondek test in order to exclude tumour.

TREATMENT

It must be stressed that the genital condition is merely one aspect of the disease, which is tuberculosis, and unless adequate treatment is given for this then surgical intervention will avail little.

Sanatorium régime, with rest, diet, and heliotherapy, is most important both before and after operation. Unfortunately, despite the national tuberculosis service which has been operative in this country since 1912, these facilities are not easily available. Before operation there is too much delay in getting a patient admitted into a sanatorium, and after operation, if a wound requires dressing or a sinus is present, there are very few places to which a patient can be sent. In this country surgical tuberculosis centres should be on the East Coast, and I only know of two places which attempt to treat surgical tuberculosis adequately, and these are at Margate and Felixstowe. At Margate the Royal Sea Bathing Hospital was a pioneer, and at both places now the London County Council have adequate establishments. For the country as a whole, however, the accommodation is hopelessly insufficient.

Tuberculin therapy has still a few advocates, but has been given up by the majority of physicians and surgeons. I have never seen any success which could directly be

attributed to tuberculin, and from my experience at the Royal Sea Bathing Hospital, where it was used in all cases by one surgeon, and never by another. I have long since ceased to regard tuberculin as of any therapeutic value.

Freshman, however, from his statistics at the London Hospital, thinks tuberculin combined with sanatorium treatment better than surgery. Hammond also advises expectant treatment, i.e. prolonged stay in a sanatorium combined with tuberculin injections, and suggests that operation should consist chiefly in ligature of the vasa to prevent extension, and that only occasionally is epididymectomy or orchidectomy called for. He has also shown that if orchidectomy is performed after puberty there is but little deterioration in general health.

Few surgeons, however, agree as to the efficacy of expectant treatment and most surgical disputes concern the merits of a conservative as opposed to a radical operation. By a conservative operation is meant epididymectomy with the removal of a portion of the vas, and sometimes ligature of the opposite vas, leaving the diseased testis, seminal vesicle and prostate alone, hoping Nature will step in and effect a cure.

Whichever type of operation is undertaken, however, the nature of the anæsthetic is most important. Pulmonary tuberculosis, latent or active, being always present, it is better to avoid inhalation anæsthesia. Local infiltration of novocain will suffice for epididymectomy, but a spinal anæsthetic should be given if a radical operation is to be performed.

Epididymectomy was first performed by French surgeons, some sixty years ago, and has remained a popular operation in France, while in Germany orchidectomy was preferred. I fail to see any great value in epididymectomy, for the testicle is diseased in the majority of cases. The advice to curette away the diseased parts, in the hope of conserving some testicular tissue because of its internal secretion, is no longer necessary, owing to the success of subcutaneous implantation of testosterone propionate, and the failure of the curette to eradicate disease is too often disappointing. An average from American statistics is 30% recurrence in the epididymis after epididymectomy or orchidectomy and in this country the average is about 40%.

Young strongly advocates a radical operation, even in advanced cases of genito-urinary tuberculosis with active phthisis. He quotes Kocher, who taught that the more diseased tissue was removed the better the body could then cope with the remainder. Sutcliffe, of Margate, certainly got better results in cervical adenitis by his operation of complete excision than others obtained by partial adenectomy and curetting. Young's operation consists in a perineal removal of the prostate and vesicles, and an inguinal removal of the epididymis and vas. He was opposed to orchidectomy, for the testis is never primarily infected, and he taught that an extension to the testis could be dealt with by the curette. He bases his operation on the assumption that infection was always primarily vesicular. In a series of 24 radical operations, he states there was genital recurrence in 3 cases, once in the kidney, whereas in 98 conservative operations (i.e. epididymectomy) there was genital recurrence in 26 cases and renal in 17. Few of his colleagues, however, obtained such good results, and the operation has never become popular.

Most surgeons agree that operation for tuberculosis of the prostate is seldom called for, unless retention is present, in which case a suprapubic cystostomy alone is advised.

The operation I favour is one I planned and carried out in 1914, and described before this Section in 1924 (*Proc. R. Soc. Med.*, 17, Sect. Urol., 60), and in the *Urologic and Cutaneous Review* in 1929. The operation is as follows: With the patient in the Trendelenburg position the bladder is emptied through a rubber catheter, which is left *in situ*, in order to keep the bladder empty. An inguinal incision is then made above and parallel to Poupart's ligament, and the oblique and transversalis muscles divided. The testis is next manipulated out of the scrotum and the vessels separated from the vas and divided. By blunt dissection the vas is traced down to the seminal vesicle, and a line of cleavage is sought for between the bladder and vesicle, which is gently separated and then avulsed from the urethra.

The chief difficulties met with are: (1) A deep and narrow pelvis. (2) Obesity. (3) Abscesses in the vas and vesicle which entail very gentle handling if rupture and spread of infection are to be avoided. (4) Involvement of the base of the bladder and ureter and dense adhesions. Hæmorrhage is seldom of serious moment. If the testicle is adherent to the scrotum and if a sinus is present, then the inguinal incision is prolonged to encircle the affected skin. The testicle with adherent skin is wrapped in gauze, and

thus contact infection prevented while the operation is proceeding. Both vesicles can be removed through the one incision.

There is often a urinous discharge for two or three days, and in two of my cases a tuberculous sinus occurred, which took some weeks to heal. Nitch is the only surgeon I know who has carried out this operation since I described it, and he finds the results disappointing, being only 6% better than epididymectomy, but the remote mortality is decreased. He found 52% apparently cured by orchido-vaso-vesiculectomy, as against 46% by the conservative operation.

Of the 13 cases I reported in the *Urologic and Cutaneous Review*, 1 died from tubercular bronchopneumonia six weeks later. There were free from symptoms or bacilli in the urine: 1 four years later, 3 two years later, 2 one year later, 5 three months later. Kidneys healthy, but cystitis with tubercle bacilli in the urine, 1 four months later. The disease was unilateral in the testicle in 7 cases, and in the seminal vesicle in 7. The disease was bilateral in 6 cases, and in 5 of these simple orchidectomy had been performed two to five years previously, so that when I operated two vesicles were removed with one testicle five times, both testes and vesicles once. On several occasions it was noticed that the ureters near the bladder were diseased.

Of a later series of 21, including these, 2 died from tubercular bronchopneumonia, an operative mortality of 9.5%. Two others died, one at eight months and one four years later. Of these 21, 17 were alive and well from one to ten years later. Nine of these had a unilateral orchido-vaso-vesiculectomy and have had no recurrence or extension (five to ten years report). In 7 cases of unilateral orchido-vaso-vesiculectomy in 1 case the other testicle had been removed six years previously, in 6, two years previously, i.e. genital recurrence or extension where simple orchidectomy had been performed occurred in 6 cases in two years, whereas in 9 cases of orchido-vaso-vesiculectomy there was no recurrence in five to ten years. In 4 cases one testicle and two vesicles were removed. I consider an orchido-vaso-vesiculectomy the most desirable operation. An epididymectomy is only justifiable if the vesicles and vas are not involved, and McGavin's findings must be remembered, that 30% of epididymes removed for suspected tuberculosis were shown on microscopy not to be tubercular. Personally I seldom diagnose a tuberculous epididymitis unless the vesicle is involved, and as I consider this to be generally secondary to the epididymitis I do not consider the delay deleterious.

In conclusion, I think that genital tuberculosis may be either blood-borne or secondary to a urinary infection; and that if secondary to a urinary infection then the vesicles are involved first. I do not consider that infection can be carried up the lumen of the vas, lymphatic extension being the usual mode of transmission. In regard to operation, if the vesicles and vas are not involved, I advise orchidectomy, but if they are, an orchido-vaso-vesiculectomy is the better procedure.

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[October 13, 1944]

Notes on Glaucoma [*Abstract*]

PRESIDENT'S ADDRESS

By P. E. H. ADAMS, M.A., M.B., D.O.Oxon., F.R.C.S.

In the course of forty-odd years of private and hospital work I have come across a great variety of types of this disease.

It is difficult to decide when the disease really starts. I have seen several cases about the age of 45 in which one has had suspicions of the discs and have kept these eyes under observation and it has not been until they are over 60 that the tension becomes raised and Bjerrum's scotoma starts and the discs look more pathological. I shall quote one case which is typical in each class. I have always used the original Schiøtz tonometer and the old scale and all the tension records given in this paper are according to that.

Senile type.—First seen in 1919, when he was 56, for presbyopic glasses. His sight was 6/6 and with + 2 J i in each eye, but left disc ? not as good as right. Tension: R. n.; L. n. I did not see him again until November, 1935, when aged 72. He had no complaints. He still had 6/6 and with + 3 D J i each eye. Both discs were a little depressed, but no actual cupping. Tension with Schiøtz was 23 mm.Hg each eye. Fields were full in each eye and showed no extension of the blind spots. However, feeling suspicious about him especially as there was glaucoma in the family, I put him on to 1% pilocarpine as a precaution.

March 1936: He had not had drops for six days. Tonometer: R. 32 mm.Hg; L. 29 mm.Hg, showing that the eyes were definitely harder. Right disc did not look so healthy as left, but still nothing definite.

I saw him at intervals up to November 1937, when the tension was R. 28 mm.Hg; L. 25 mm.Hg.

The tension varied from R. 27 mm.Hg; L. 23 mm.Hg, up to April 1941, four years later, when the tension was, R. 33 mm.Hg; L. 29 mm.Hg. No drops since night before.

January 1943: Tension: R. 33 mm.Hg; L. 26 mm.Hg, but still no loss of field. But April 1944, when he next reported, he was now aged 81:

Vision: R. 6/6 + 2.5 J i; L. 6/6 + 2.75 J i. Tonometer: R. 48 mm.Hg; L. 33 mm.Hg. No drops that morning, but he had his eserine the night before. Fields still showed no extension of blind spot, but tension was obviously getting really hard in the right eye.

August 1944: Tonometer: R. 40 mm.Hg; L. 28 mm.Hg. Taken three hours after his pilocarpine drops. Blind spot in right eye a trifle larger than left for the first time, but no extension observed with Bjerrum screen at one metre. I then put him on to pilocarpine 2% b.d. and eserine gr. 1 in oil at night, right eye.

This patient is a medical man, he is very averse to having an operation if it can possibly be avoided. Theoretically of course the right eye should be operated on and I have explained this to him, because in my experience these cases may carry on quite well for an indefinite time and then rather suddenly there is a definite deterioration in their sight, which is permanent. The difficulty is added to by not knowing how long one has

to cater for. Although this patient is 81, he looks about 60, is still working to a moderate extent and doing his rounds on a bicycle now. At times after trephining, even after the most successful operation, some clouding of the transparency of the lens may occur, leading to considerable loss of sight. These unpreventable happenings after filtration operations are what makes the problem such an anxious one as the actual sight before operation is so good. With a cataract the sight is already so defective that even if things do not go well, the patient has not lost so much, but when operating on an eye with 6/6 vision, if the patient ends up with vision of say 6/60 he is naturally not too pleased. These senile cases seem to tolerate increase of tension better than the ones seen in middle age.

One objection to miotic treatment in these cases is that they are frequently complicated by lens opacities and, when central, the small pupil causes so much inconvenience, especially in the mornings when they are busy, that it is difficult to induce the patient to use the drops faithfully.

There is another rather similar type of case in which the discs look suspicious when first seen. It is watched carefully but it remains on the border line, e.g.:

F. J. W., aged 50. First seen in 1914 (thirty years ago). Both discs well-marked circular physiological cups. Tension: R. n.; L. n.

I saw him last in May this year; he is now 80. His vision corrects to: R. 6/6, J i; L. 6/6, J i. Tonometer: R. 26 mm.Hg; L. 23 mm.Hg. Fields full, no extension of the blind spot, but the cup in the right eye is definitely more extensive than it was, and in both eyes the nasal edge of the cups is thin and sharply cut.

This is a borderline case suspicious from the first but no further development up to the present.

An example of guessing wrong in a case of this sort is the following.

N., May 22, 1919, aged 80. He had been operated on for glaucoma some thirty years before, wide iridectomies having been done. No obvious filtration. The left eye was blind, the disc being quite atrophic and grossly cupped. The tension in the right eye was not appreciably raised to the finger. The disc showed some cupping. Vision: R. with correction 6/12, and with presbyopic correction J ii and J iv. The field was contracted, with a notch on the nasal side almost up to the fixation point.

March, 1922: He had a much contracted field, only one eye, and he was 83.

I decided to let him carry on under miotics. He personally was averse from further operation.

June 1926: Still alive at 92, well and strong, but alas, almost blind. He did not die for three and a half years after that and was by then quite blind.

There is another type of case which is characterized by very high tension, but no history of blurs or rings of colour and eyes perfectly quiet. The tension is often higher than one meets with in acute glaucoma and yet nothing to show for it.

Miss B., first seen in 1923, aged 42. Vision: R. $6/6 + 1 = 6/6 + 2$ J i; L. $6/9 + 1 = 6/6 + 2$ J i. Discs and fundi healthy.

March, 1935, aged 54: R. $6/60 + 2.5 = 6/6 + 4.5$ J i; L. $6/60 + 3 = 6/6 + 5$ J i. No change noted in discs and fundi.

I did not see her again until June 1944, aged 63. She was then complaining that the sight of the left eye had failed 4/12. Under her own doctor for anaemia and being generally run down and had had much worry. She had had no pains or headaches and no mists or blurs. Vision: R. $6/60 + 3 = 6/6$; L. $6/60 + 3 = 6/18$. Left disc had an extensive temporal cup with upper edge sharply undermined; arterial pulsation well marked. Right disc no cupping; some thickening of inferior temporal artery, but tonometer: R. 50 mm.Hg; L. 65 mm.Hg.

Field in left eye showed only a small central field with an extension up and in on the temporal side. (Chart 1.)

Right field was quite full and no extension of the blind spot.

It does seem remarkable that no symptoms other than failure of sight in the left eye had been noticed and the patient was firmly convinced that there was nothing amiss with the right eye. In this case eserine had very little effect on the tension and did not cause much contraction of pupils. It was obvious that nothing but operation was indicated in this type of case and this has now been done to both eyes.

Cases of acute glaucoma with premonitory symptoms extending over many years are not of frequent occurrence:

Mrs. W., aged 37, came to see me December 1912. She stated that pains came on over

her eyes after working for half an hour and that the room seemed full of smoke. She also noticed that the lights had rings of colour round them at night but never in the morning. She had noticed this for five years. Her vision was R. 6/6; L. 6/6; with 1D of hypermetropia.

The discs had only central physiological cups, and tension was apparently normal. I took her tension with the tonometer, and found it to be 24 mm.Hg. I then got her some fine sewing and sat her down to this for half an hour. At the end of that time I found her pupils semi-dilated, corneas slightly steamy, and tension up to 40 mm.Hg each eye. On putting in a drop of eserine, gr. j, ad $\frac{1}{2}$ j, the corneæ rapidly brightened and the tension came down to normal. Operation was declined, and she was given eserine drops, when she had had several more attacks. She had been worried by her husband's illness, and reported at intervals of three months with no further mists until December 1913. One bad attack came after a tooth extraction. If she sat by the fire the side next the fire had the attack.

March 1917: Four years later I saw her again. Vision: R. $6/6 + 1.5 = 6/6$; L. $6/5 + 1.5 = 6/5$. She found that going out in the dark brought on an attack of mist, and on coming in and standing under a brilliant light with a paper to reflect the light into her eyes, the attack passed off.

November 1930, aged 56: Her eyes were keeping all right with the drops. If it was a dark day she used one drop midday and always one at night. In summer only one drop at night was necessary. She said her eyes always came over misty if she went out walking and it got dark; she then put a drop in and the mist cleared up. She had had one bad attack last winter and one this winter (1930).

Vision: R. $6/12 + 1 = 6/6 + 3$ J i; L. $6/9 + 1 = 6/6 + 3$ J i. Left disc looked a little more cupped than the right. Both anterior chambers were a little shallow. Tonometer: R. 25 mm.Hg; L. 27 mm.Hg. Fields were full without apparent extension of the blind spots.

She still declined operation, though realizing that the time would probably come when it would have to be done. I have not seen this patient for many years, so cannot tell you the end of the story.

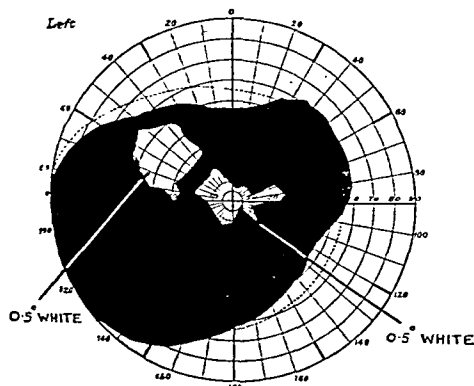


CHART 1.—Miss B., July 11, 1914.

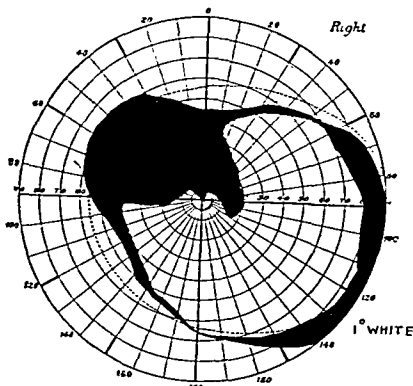


CHART 2.—J. W. H., March 26, 1943.

There is the type which might be called chronic acute glaucoma, in which there are occasional attacks of mists and blurs with rings of colour round lights, but the acute attack which does not respond to treatment may be delayed for years, perhaps for ever, but gradual loss of field occurs as it does in chronic glaucoma.

One patient, J. W. H., a man, started these symptoms at the age of 42, in the left eye. He had no cupping of discs but the attacks became more frequent but were always relieved by a drop of eserine. Eventually I trephined him after about a year of these attacks, and this was in 1917, and his eye has kept perfectly well ever since. His other eye kept well but had occasional attacks of blurring in it, but field and vision kept all right until 1943, when after a three-year interval, very much ashamed of himself, he came up and said that he had noticed that the right eye was dark above. He had lost all the upper nasal quadrant of his field, the tension was raised to 42 mm.Hg, so this eye was also trephined. He never had an acute attack or any redness or pain, only blurs and rings of colour with an occasional ache. These cases differ therefore in a way from the ordinary premonitory signs which often occur before an acute attack materializes. (Chart 2.)

As regards physiological cupping, when these cups have very sharp edges I am always

rather suspicious about them although they may be quite central with good healthy looking margins.

The following case, Mrs. E., first seen in January 1943, shows that they may be the early stage of pathological cupping.

She was a woman aged 60 who complained of tired eyes. She had had her present glasses five years and was not seeing so well with them as she had done. Both discs had sharp cut but quite central circular cups. Vision corrected to 6/6 and J i with each eye. Taking the tension I found it: R. 30 mm.Hg; L. 25 mm.Hg. I took the fields which were quite full but there was some slight enlargement of the blind spot in the right eye, but not in the left.

Things kept quite steady until March 1944, then tension: R. 25 mm.Hg; L. 20 mm.Hg. Both eyes then showed a small Bjerrum scotoma more pronounced right than left, so I advised operation, and now both eyes have been successfully trephined. The discs have still only central cups, but the upper edge of the cup in the right eye is sharply cut and undermined.

This brings me to another very interesting case, showing how an eye can withstand a constant raised tension for very many years with only a very gradual deterioration of vision when the trouble starts at an early age.

P. This patient first saw R. W. Doyne in 1902, being then 28 years old. He had noticed that the sight had not been so good for about the last five years. For the last two years he had seen rings of colour round lights with temporary attacks of misty vision. No pain. R. W. D.'s notes: Both eyes buphthalmic; T. + 1 in both. Very marked arterial pulsation in the right eye and slight in the left. Both discs deeply cupped, left one the worst. Vision: R. 6/60 - 1 = 6/12; L. 6/60 - 1 = 6/36. He was put on eserine twice a day.

February 22, 1931: Vision: R. 6/60 - 2 = 6/24 (ii) + 2 J iv, with hand magnifying glass J i. Tonometer: 40 mm.Hg.

This patient then had had a very high tension in the right eye for thirty years, and yet he could still read and his field has only come in very gradually, but ten years later he was practically blind.

This next is rather a peculiar case of glaucoma which I was asked to see by the neurosurgeons.

He was admitted into hospital under them for a horizontal hemianopia and they could not localize any lesion which would account for it, the upper halves of each field having been lost. I found that the discs showed extensive but not deep cupping, and with the tonometer the tension was: R. 32 mm.Hg; L. 32 mm.Hg. On taking the fields I found that the upper halves of each field (Charts 3a and 3b) lost with extensions from the blind spot up to this area, and that chronic glaucoma and not an obscure cerebral lesion was the cause of the condition.

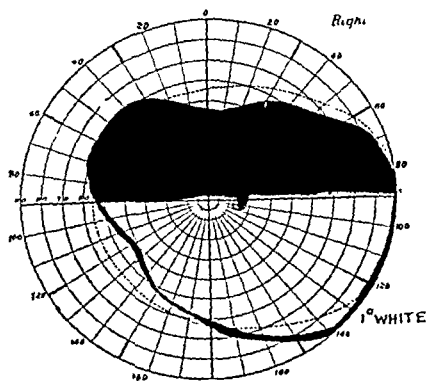


CHART 3a.

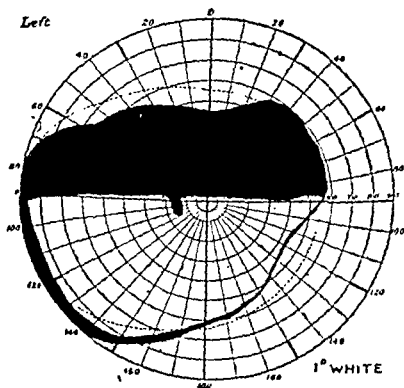


CHART 3b.

Chronic glaucoma is a progressive condition sometimes so slow as to be almost imperceptible, though more ordinarily progress downhill is fairly rapid. I have never seen the tension in advanced chronic glaucoma go down and become subnormal until this year:

Mrs. W., first seen in February 1940, aged 69. She had had an attack of shingles on the left side of her head in December 1939. Left eye was still tender and cornea anæsthetic. Left disc shows extensive shallow cupping. Tonometer: R. 22 mm.Hg; L. 32 mm.Hg.

June 1940: Tension the same. Fields then taken. Vision: R. $6/24 + 1.5 = 6/6$; L. $6/36 + 1 = 6/24$. Right field full. Left field much contracted.

August 23, 1944: Tonometer: R. 32 mm.Hg; L. 14 mm.Hg. Using pilocarpine 1% o.n. to both eyes. No extension of blind spot in right eye but she is not a good patient for this purpose. The left eye looks all right, there is no sign of shrinking, but the tension has fallen from 32 mm. to 14 mm.

I think there is no doubt she had chronic glaucoma in the left eye before the attack of shingles. Whether this has any connexion with the fall in tension I do not know. I never remember noticing low tension in an eye following on an attack of herpes.

I have sometimes been asked how long one can keep an eye on miotic treatment. My record is a Miss L., first seen 1908, aged 50, reported in my Doyne Memorial Lecture in 1931, and still alive aged 86. Her right eye was practically blind when I first saw her, and she declined operation on her only eye. If one had known that she was going to live so long one would have somehow persuaded her to undergo operation. At the same time, thirty-six years have gone since she first started on drops and she can still read. Her field, if compared with the one taken in 1933, shows that the increase in the defect has not been very great (Charts 4 and 5). As to preservation of sight after operation I have one case of trephining done in 1917 and his lens has kept clear and his vision to-day is: L. $+4 + 1$ cyl. axis 160 = 6/9 and $+7 + 1$ cyl. axis 160 J; i.e. as good as ever.

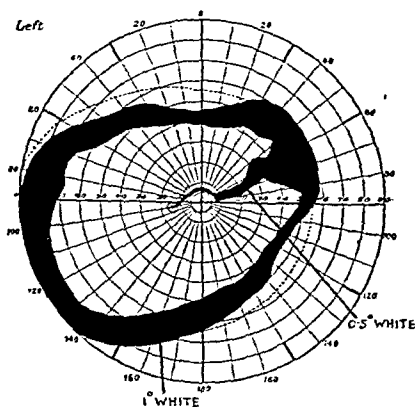


CHART 4.—Miss L., May 26, 1933.

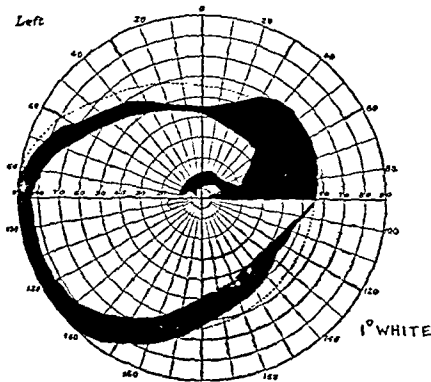


CHART 5.—Miss L., October 2, 1944.

I have done trephining, iridencleisis, Lagrange, and, like most other people, I once devised an operation of my own, which was called the H.A.L., but trephining was the operation I chiefly used and I imagine that there is no complication which I have not met with or suffered from.

Non-reformation of the anterior chamber is the one that has really interested me most, it is of very common occurrence after trephining, and is of course associated with detachment of the choroid to a greater or less extent, it may only last for two or three days, on the other hand it may persist for a month or so and then reform. I have never quite understood what is at the bottom of the condition as it is not due to persistent leakage of aqueous, the conjunctival flap is firmly adherent, there is no watering or irritation of the eyes, but there is no raised bleb over the scar as there should be and the eye is very soft. It is as if all the secretions of aqueous had ceased and the eye gone to sleep as it were. After a varying interval the anterior chamber gradually fills up, the detached choroid goes back into place and as a rule, all is well. As regards treatment, if this condition persists I have found 2 or 4% dionine drops have a beneficial effect in some cases. There is no

rather suspicious about them although they may be quite central with good healthy looking margins.

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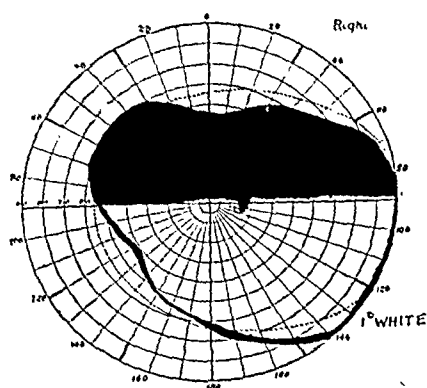


CHART 3a.

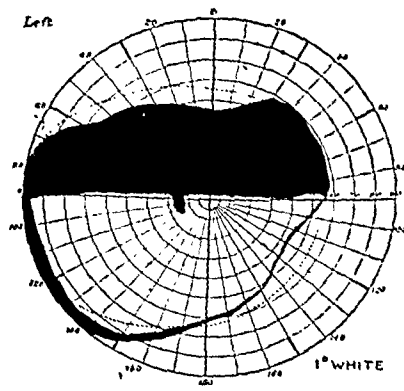


CHART 3b.

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Last year, for the first time, after twenty-five years of experience of the operation in private and in hospital, an eye had been obtained post mortem for examination, and his colleague, Mr. E. Wolff, with some very good sections, had substantiated by histological proof the correctness of his previously published presuppositions. A joint paper would shortly be published on the subject.

Mr. Williamson-Noble asked whether the patients were put on pilocarpine after the operation.

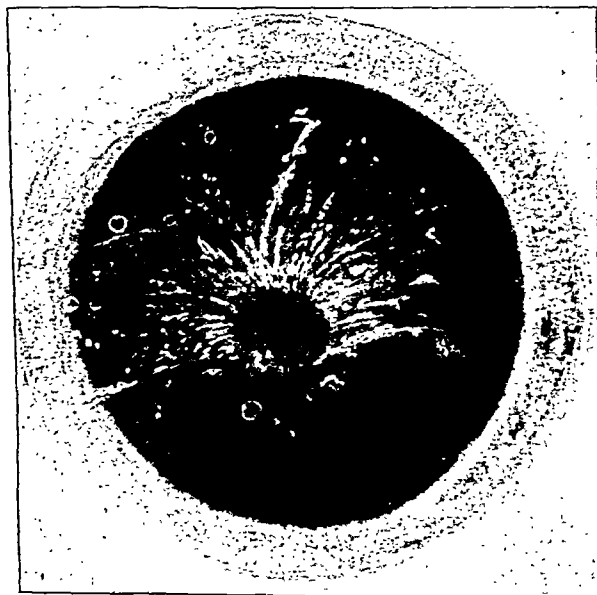
Sir Richard Cruise said that with confidence atropine was instilled for the first week, to ensure as far as possible that all filtration of aqueous should take place through the incisions and not through the normal channels.

Mr. Eugene Wolff said that an endeavour had been made for some twelve years to obtain a section of an eye operated on by this sclerotomy method. There was never occasion to remove one of these eyes from the living patient. Eventually a patient who had been operated on some years before died, and the eye was obtained and sent to the laboratory. There could be no doubt that the track was lined with endothelium. It was usually stated that following an operation no such lining took place, but in this case the lining was obvious.

Three Sisters with Familial Corneal Dystrophy.—V. M. ATTENBOROUGH, D.O.M.S.

Mrs. Attenborough said that she saw this family first in 1943. Two of the sisters attended the out-patients' department at the Western Ophthalmic Hospital, and the other was a patient at Moorfields. She had drawings made of their eyes, hoping that later she could collect other members of the family. In February of this year there was a report of some observations on hereditary corneal dystrophy (J. R. Mutch, *Brit. J. Ophthalm.*, 1944, 28, 49). These cases, she thought, belonged to the class which was classified there as granular corneal dystrophy, a dominant disease affecting both males and females. The opacities, which were always bilateral, occurred as discs or rings situated beneath the epithelium in the axial region of the cornea.

The speaker showed three drawings of the condition in the sisters (one of which is shown fig. 1). The eldest was aged 24, with onset at about 18; vision right and left 6/9.



From coloured illustrations by J. Bayes.)

Familial corneal dystrophy. Female aged 21

object gained in keeping these patients in bed and I have thought that getting them up and letting them move about was helpful.

I had one case in which the condition relapsed three months after operation but recovered completely in four months.

Another fact that has impressed me about operations on the eye is that if one eye behaves in an unusual manner, the other eye is quite likely to do the same thing.

For instance, I trephined a chronic glaucoma case; he was a healthy man of about 60, the operation went off quite satisfactorily, but next day he had a large hyphæma which slowly increased during the next couple of days until it occupied about two-thirds of the anterior chamber and there it remained. I kept him quiet in bed and he was a very good patient, the eye kept quite free from inflammation and settled down quickly and he had a perfectly white eye, but with the hyphæma filling half the anterior chamber. Eventually I did a paracentesis and evacuated the blood, there was no further bleeding and he was able to go home in a few days. Some months later I had to trephine the other eye. Exactly the same thing happened, ten days after the operation the eye was quiet but the anterior chamber half full of blood. I did not wait any longer, did a paracentesis and the eye again showed no reaction and the patient went home a couple of days later.

I have never met this complication before or since, it may be common, but it was my only experience of it.

Another more tragic example of the similar behaviour of the two eyes is the following case.

He was a medical man, and a myope with obstinate chronic glaucoma not controlled by miotics. He was also the subject of severe rheumatoid arthritis and was more or less crippled. Following an uneventful operation, at the end of forty-eight hours there was a tremendous reaction, an intensely red eye with the iris very hyperæmic and accompanied by great pain. The pupil did not become adherent but would not dilate properly. After a few weeks the inflammation subsided but the transparency of the lens was spoilt and the sight much diminished.

The other eye was deteriorating and so after a careful vetting and general treatment, I trephined the other eye, operating with the greatest care and gentleness to avoid a too sudden loss of aqueous or undue trauma, but at the end of forty-eight hours exactly the same condition developed possibly even more violent than in the first eye and with the same unfortunate result.

In recording the cases which have been treated with miotics for many years, I do not want to give the impression that I consider this to be the correct treatment for chronic glaucoma. Once the diagnosis has been made and the effect of miotic treatment determined, unless there is any definite contra-indication, operation should be performed, and the younger the patient the sooner it should be done.

Hinge Flap Sclerotomy Drainage Operations. Three Cases.—Sir RICHARD CRUISE, G.C.V.O., F.R.C.S.

Sir Richard Cruise said that he had shown these three cases as typical results of his method for the relief of tension in the hope that they would interest members who were not entirely satisfied with their results in other operations for chronic glaucoma.

The principle he aimed at was to establish a permanent filtrating cicatrix without excision of any tissue.

To attain this the incisions were deliberately prevented from normal healing by connective tissue, to enable the endothelial cells lining the anterior chamber to proliferate into and round the margins of the incisions, so that when healing did take place the cicatrix was formed of endothelial and connective tissue cells. The margins of the hinged flap were prevented from sealing down by massaging the aqueous out of the anterior chamber underneath the conjunctival flap, thereby causing the corneoscleral hinge flap to ride up under the conjunctival bulge. It was essential to do the first dressing and manipulation eighteen to twenty hours after the operation, otherwise the incisions might be firmly healed.

An account of the operation appeared in the *Trans. Ophthal. Soc. U.K.*, 1940, 60, 33.

Sir Richard had been practising this method, with modifications of technique, for twenty-five years, and the results were extremely satisfactory. There was minimal damage to ocular tissue, and complications were negligible. Cataract, iritis, hemorrhage, delayed formation of anterior chamber, and late infection did not occur.

Last year, for the first time, after twenty-five years of experience of the operation in private and in hospital, an eye had been obtained post mortem for examination, and his colleague, Mr. E. Wolff, with some very good sections, had substantiated by histological proof the correctness of his previously published presuppositions. A joint paper would shortly be published on the subject.

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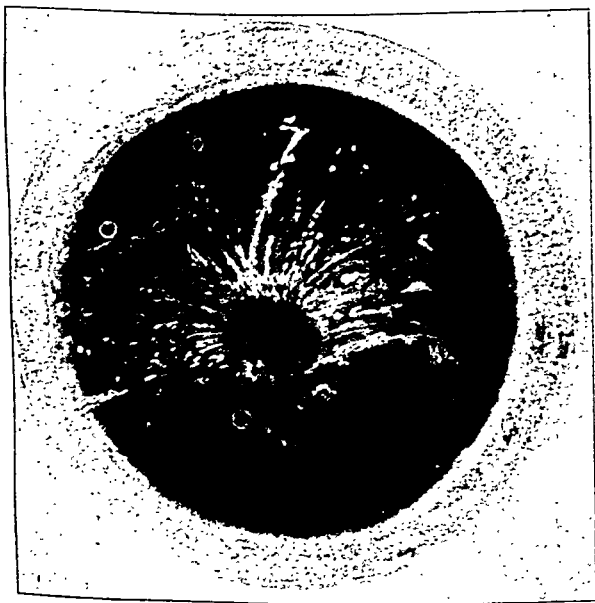
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From coloured illustrations by J. Bayes.)

Familial corneal dystrophy. Female aged 21

The second girl was aged 20; onset at 13; vision right and left 6/24. The youngest was aged 14; onset at 11, vision right and left 6/24. The rings were present in all three cases, but were most marked in the second of the three girls. She thought that the fact that the onset in the eldest girl was not noticed until 18 was probably due to the fact that her vision was better. The opacities for the most part lay beneath the corneal epithelium and Bowman's membrane, but some also lay deeper in the corneal substance. The father, grandmother, and great grandfather were known to have been affected.

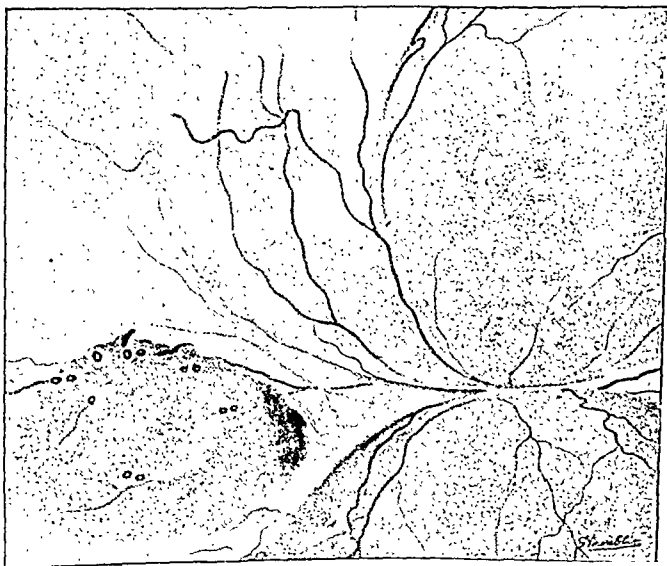
Retinal Detachment with Raised Tension.—H. G. W. HOARE, F.R.C.S.Ed. (By courtesy of Mr. STEWART MACKY.)

The patient was a man aged 42, apparently in good health. Fourteen years ago, while engaged in his occupation as a sawyer, a piece of timber 3 in. cube flew up and struck him in the right eye. The sight was hazy for three days, but there was no bleeding from the eye, nor was there a black eye. He was attended by the works' nurse, but did not seek medical advice. Three months later he noticed a waviness in the sight of the right eye, first observed while at rest after his day's work. He consulted an oculist, who prescribed glasses. The sight of the right eye gradually deteriorated, the central vision being lost before the peripheral vision. He was quite blind after two years; that was some twelve years ago. He had never had pain in the eye, nor had he had any trouble with the other eye. Six weeks ago he underwent a medical examination for the Army and was asked to seek a specialist's opinion. In this way he came under Mr. Macky's care.

Present condition.—Left eye vision 6/6 with correction, appearing to be normal. Right eye: no P.L. Pupil inactive to light, but reacting briskly consensually; the tension was + +; there were slight posterior cortical lens changes, otherwise the media were clear. There was a complete shallow retinal detachment which was not wavy, no hole was seen, and no new growth. The disc was markedly cupped.

Hæmorrhagic Coats's Disease.—A. J. B. GOLDSMITH, F.R.C.S.

Boy aged 10 years. It was noticed that the right vision was defective in November 1943. There was nothing in the family history nor in the personal history except an attack of whooping-cough in March 1943. Nothing abnormal was found in the general



Hæmorrhagic Coats's disease.

physical examination. A skiagraph of the chest showed increased hilar striation, thought to be a legacy of the attack of whooping-cough in 1943. The Wassermann reaction and Kahn and Mantoux tests were all negative, and the blood-count was normal. In the right eye there was a total retinal detachment, and the surface of the retina was covered with glistening bodies, probably cholesterol crystals. In the lower temporal quadrant there was a massive retinal exudate on the surface of which there were multiple punctate and diffuse hæmorrhages (see fig.). The vessels in this region showed many varicosities. The case seemed to be an example of the first group into which Duke-Elder (*"Text Book of Ophthalmology"*, 1940, 3, 2610, London) classified Coats's disease.

Mr. R. Affleck Greeves agreed with the diagnosis. The varicosities were commonly seen and were characteristic of Coats's disease. He did not therefore agree with the suggestion of another speaker that the condition might be due to whooping-cough.

Mr. Goldsmith, in reply to questions, said that the patient had been under observation only for a fortnight, but that the whooping-cough was in March 1943, and the defective vision was not noticed until November 1943, although, of course, it might have existed before that.

Five Cases Shown by VICTOR PURVIS, M.B.

Case I.—Loose Flocculus in Anterior Chamber.

A man, aged 20, had noticed a loose floating black spot in his right eye. He was found to have a loose spherical piece of material in the anterior chamber of the right eye, about 1 mm. diameter, which could be displaced in the anterior chamber to any point desired. It was seen on the back of the cornea when his head was forward; if he held his head back the piece of pigment floated on to the iris or lens. He had a normal iris and normal pupil but this piece of material looked like a ball of pigment under slit-lamp examination, and could only be assumed to be a congenital abnormality. It did not interfere with vision in any way, and he did not feel any pain, but it was now causing some functional worry. He had not heard of nor seen any similar case where the pupil margin was normal.

Mr. C. B. Goulden said that he had seen a number of these cases. They were cysts of the pupillary marginal pigment. He had also seen one in a black spaniel.

Mr. Frank Law endorsed this opinion. He recalled a case, seen a few years ago, which he had examined on the slit-lamp and had come to the conclusion that it was cystic. Crawford had a paper on the subject in the *British Journal of Ophthalmology*, 1944, 28, 410. These bodies were well developed in the horse, and there they were known as corpora nigra.

Case II.—Glass in Anterior Chamber.

Woman, aged 54, had a piece of glass in the anterior chamber. An attempt had been made to remove it, and the question was whether another attempt should be made. Under the capsule of the lens, a movement of the soft lens matter was visible under the slit-lamp. One assumed that the soft lens matter was mobile and that the case was becoming morgagnian. Mr. Purvis could not remember having seen such mobility before.

Mr. W. E. Heath, who was associated with Mr. Purvis in Case II, was asked what was the technical difficulty in removing the piece of glass, and said that the glass was lying around in the angle of the anterior chamber at about the position of 6 o'clock. He inserted a keratome into the angle of the anterior chamber and hoped to remove it, but there was a certain amount of wedging between the lens and the cornea and he was unable to make the extraction. He then tried to do an iridectomy, but the glass prevented him from getting effective hold of the iris.

Asked how long the glass had been in the eye, he replied that the time which elapsed between the case coming in and the attempted operation was ten days.

Mr. Frank Juler referred to a case (*Trans. Ophthal. Soc. U.K.*, 1930, 50, 118) from which he had removed a splinter of glass which was free in the anterior chamber. He had made an incision as for Saemisch's section with the patient facing and looking downwards; the ensuing aqueous drip carried the splinter into the section, whence it was easily picked out after the patient had resumed the usual position on his back. In a similar case recently he had improved upon the technique by making a puncture with a broad needle in the usual position; the patient was then turned over so that he looked downwards; a touch on the cornea released the aqueous, and the foreign body was recovered from the lower fornix. In this case the minute body was of a non-magnetic metal.

Dr. John Marshall suggested that in a case of non-magnetic foreign body in the eye a corneal section downwards, such as Dr. Traquair employed in his intracapsular extractions, gave a good approach to the angle of the anterior chamber. A suture was placed in the conjunctival flap, and the cornea turned upwards so that the major portion of the iris was exposed, and the foreign body could be extracted by blunt forceps with ease.

Case III.—Persistent Pupillary Membrane.

This was a gross case of persistent pupillary membrane with strands coming forward and attaching themselves to the back of the cornea.

Cases IV and V.—Massive Exudative Retinopathy.

These were two contrasting cases of exudative retinopathy, one in a woman of 43 and the other in a woman of the more usual age for such cases, namely, 69. The right eye in the second case gave a clue to the cause, showing an early central degeneration. The left eye showed an extraordinary mass which looked at first like a neoplasm and in fact had been so diagnosed; but the picture taken as a whole, with the hæmorrhages, confirmed the diagnosis of exudative retinopathy.

The first case showed a central white mass under each retina. This was a youngish woman who was otherwise perfectly healthy.

Section of Odontology

President—H. T. ROPER-HALL, M.B., M.D.S.

[October 23, 1944]

Jacobson's Organ

PRESIDENT'S ADDRESS

By H. T. ROPER-HALL, M.B., M.D.S., M.R.C.S., L.D.S.

(From the Department of Anatomy, University of Birmingham)

JACOBSON'S organ (the vomeronasal organ) was fully described by Jacobson (a Danish anatomist) in 1811; although Ruysch, in 1703, showed interest in it.

It is a paired structure, lying on each side of the nasal septum in the anterior part of the nose, just above the palate and varying in size from rudimentary to large according to the animal; it exists completely in human intra-uterine life, is rudimentary in adult man and other microsomatic animals, but is always well developed and functioning in the macrosomatic animals (Lenhossek, 1912).

The organ is tubular and consists in humans of a small opening on the nasal wall which communicates by means of a short tubular portion with the body; both entrance and interior of the organ are lined with cylindrical and ciliated epithelial cells of special sensory type; its general structure is similar in most animals, but there are important variations in anatomy. Always present and usually surrounding the organ is a tube of cartilage which differs in its shape and relationship in various animals.

There are three general anatomical arrangements of its duct: (a) As in man, monkey, &c.; with the anterior opening on the nasal septum. (b) As in horse, camel, pig, &c.; within the upper part of the incisive canal. (c) As in ox, &c., and some reptiles—on the anterior part of the palate just within the orifice of the incisive canal.

The arrangements (b and c) ensure a direct relationship between the mouth and Jacobson's organ.

From the human dental point of view Jacobson's organ is interesting as it lies closely above the incisive canal and incisor teeth, and because it has been asserted that mid-line cysts of the premaxilla may arise from aberration of its vestiges.

DEVELOPMENT

In humans, Jacobson's organ develops at a very early age in embryonic life (8 or 9 mm.) in the primitive nasal cavity, on the medial side of the olfactory pit, which corresponds to the nasal septum.

It is first a shallow depression which in embryos of larger size is gradually transformed into a groove directed backwards, and afterwards becomes gradually closed from behind forwards, and only the anterior end remains open (*see* later description of 12.5 mm. stage).

In early human embryos this epithelial tube has a fairly wide communication with the nasal cavity, and it is comparatively long; e.g. according to Paulet (1907) the length of Jacobson's organ in a 13.8 mm. human embryo is 0.35 mm. (length of groove and tube in 12.5 mm. embryo is 0.220 mm.). Brandt (1938) offers some useful observations on the calculation of the size of Jacobson's organ.

POSITION

The organ (in humans) consists of a pair of epithelial, elongated sacs enclosed in a cartilaginous capsule situated on the nasal septum and extending along it above the incisive canal; it is a narrow canal in the epithelium of the nasal septum 5 to 7 mm. long and directed horizontally backwards about 10 mm. above the floor of the nose, and opening anteriorly above the nasal spine.

An illustration is to be found in Ruysch and Sömmering (Franke).

JACOBSON'S CARTILAGE

Each Jacobson's organ is partially or entirely covered by a fine cartilaginous protective lamella; this cartilage puckers the mucous membrane of the nasal septum and the resulting bulge helps to locate the organ (Lenhossek, 1912).

These cartilages are variously described as the vomerine cartilage of Huschke; the accessory nasal cartilages of Sappey; the ploughshare cartilages of Jacobson; paraseptal

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exists which closes the incisive canal when desirable; he concludes that the organ is an accessory organ of smell and that scents come to it in a serous liquid.

In view of the powerful connexion between the olfactory receptors and the subcortical centres which exist in animals in contrast to man, Milstein (1929) concludes that odour as represented by Jacobson's organ must be connected intimately to the subcortical centres of sexual life and with other important centres (e.g. feeding).

COMPARATIVE AND HUMAN

(a) *Comparative*.—Jacobson's organ exists extensively among vertebrates, and where it is absent, there are often embryonic rudiments.

This special area of the olfactory organ is highly developed in all herbivora, in which the incisive canals are widely open and thus the juices and odours of the mouth have free access to the organ; the incisive canal may be considered the original connexion of the primitive choanæ (Parker).

Fishes.—These have an olfactory organ of a double character which may be the fore-runner of Jacobson's organ; in elasmobranchs a supplementary olfactory organ arises in connexion with each nasal passage and thus with the mouth (Neal and Rand).

Amphibia.—McCotter (1917) says that the vomeronasal organ in frog is a cup-shaped structure that lies at the medial extremity of the inferior nasal chamber and communicates directly with it laterally.

Reptiles and birds.—In snakes and lizards the organ, which opens in the mouth, is a finer sense organ than the olfactory organ proper and is clearly differentiated from the true organ of smell (Pearlman) (Symington, 1891). There is in birds a little recess in the nasal cavity which would correspond to Jacobson's organ of the mammals. The organ was thought to be absent in reptiles until Howes (1891) discovered a pair of cartilages in the anterior part of the nasal cavity which he thinks may be the cartilaginous sac of Jacobson's organ; he concludes that the accepted principles of morphology forbid our looking upon Jacobson's organ of reptiles and mammals as in any way distinct; Corning states that Jacobson's organ in reptiles achieves a high degree of development; Pearson (1921) examined a late foetus of *Lygosoma* species 4.8 mm. in length and found Jacobson's organ present within its cartilage.

Monotremata.—Symington (1891) discussing *Ornithorhynchus* says that a bristle passed from the mouth into the incisive canal enters a cavity which extends backwards for some distance in relation to the nasal septum; this is Jacobson's organ which is partly surrounded by a cartilaginous tube continuous with the floor of the nose. Symington thinks that Jacobson's organ attains its highest development in Prototheria; he states that in all mammals so far investigated the opening is anterior to the cavity of the organ, but in *Ornithorhynchus* Jacobson's organ extends forwards from the orifice as well as backwards.

Typical mammals.—In the Horse the nasal opening of Jacobson's organ is just within the incisive canal (Minett). Camel, opens in top of incisive canal (Minett). Ox, 8 or 9 cm. long, opens within incisive canal; near nose or near palate according to breed (Minett). Pig, 2 to 3 cm. long, opens in incisive canal close to palate (Minett).

Morphological.—The organ is present with its cartilage in hyrax, and Broom (1898) suggests that this organ may prove to be a very useful study of affinities between hyrax and rodents; he says the snout of hyrax is not of mammalian form and the palate is something like that of wombat and other Marsupials, but from his observations of Jacobson's organ Broom concludes that hyrax is similar to the Ungulata and nearest to sheep and ox.

From the above notes the conclusion is justified that Jacobson's organ is widespread throughout all vertebrates.

(b) *Human*.—In man the organ is found some distance above the palate and opens directly into the nose.

Watson-Williams (1910) says that although a small tubular recess, corresponding with the situation of Jacobson's organ has been stated to occur occasionally in adult man, he has never met with anything of the kind; on the other hand, Browne (1899) says Jacobson's organ can be demonstrated in man about 1.5, but is of vestigial interest only; he quotes Kölliker—average situation is 8.5 mm. above floor of nose and 24 mm. from junction of membranous septum and lip.

Franke says that Jacobson's organ in the adult is 5 to 7 mm. long and about 10 mm. above floor of nose, opening anteriorly above the nasal spine.

Keith ("Human Embryology and Morphology", 1933) has an illustration on page 228 showing its relation to the incisive canal; he states that in the human foetus the organ is at its maximum at the fifth month and afterwards usually only vestigial. He also shows (1909 Edition, fig. 13) the preparation No. 169 in the Royal College of Surgeons'

cartilages of Tyurgat or recurrent cartilages of Parker; they should not be mistaken for Jacobson's organ itself. Franke (1921) proves that they are the same structures in man as in other animals.

These cartilages (in humans) far outstrip in length the remains of the organ of Jacobson on both sides, and at the anterior end run out into many spurs, but they are undoubtedly the homologues of the cartilages which enclose the organ of Jacobson (Kölliker, *see* Franke).

Weber (1904) says "Jacobson's cartilage detaches itself from the floor of the cartilaginous nasal capsule at the side of the septum; it loses its junction with the posterior part of the capsule in Marsupials (Teydel), but in mammals the anterior part usually remains in contact with the septum; it thus appears to rise from the anterior part of the septum and to extend free backwards".

Hamlin (1930) suggests that Jacobson's cartilage has two actions; one like the thoracic wall to prevent collapse when internal pressure is reduced and the contents expelled, and a second to facilitate a rise in internal pressure by preventing expansion of the organ at the time this pressure is being developed, thus favouring a complete ejection of its contents.

Nerve supply.—The nerve supply is derived from at least three sources: olfactory, trigeminal, and the sympathetic system.

Minett (1925-26) says that in the horse the nerve supply is from the olfactory and sphenopalatine nerves.

Olfactory filaments have been observed by Read (1908), Milne Dickie (1914), Franke (1921), Denker and Kahler (1925), and Hamlin (1930); fifth cranial (trigeminal) nerve elements by Franke (1921), Kölliker (*see* Franke), and Parker (1922); sympathetic elements by Keith (1933).

Denker and Kahler (1925) say that the organ is supplied by the terminal nerve, the same sensory nerve which supplies the organ of smell in fishes, and Buchanan (1916) states that in ruminants there is a direct nerve supply to the organ from Meckel's ganglion.

Function.—Jacobson's organ appears to have no function in man, but in other animals it assists in the selection and recognition of suitable foods and acts as an important supplementary organ of taste and smell. Animals have patent incisive canals and thus juices and odours have free access to Jacobson's organ (Keith, 1933).

Although it is joined by filaments of the olfactory nerve it can scarcely be supposed that the organ has merely the same function as the olfactory area itself; the usual theory is that it represents an accessory organ of smell; it is rather unlikely that the inspired air reaches its special sensory cells, because in several animals the organ joins the oral cavity.

According to Carlier, the organ helps in touch. Cuvier says it is an organ of smell and helps animals to tell which foods are poisonous; Gratiolet that it is important in detecting sexual smells; Carlier that it enables animals to acquire a notion as to what objects surround them, and Hamlin (1930) that its function may be to distinguish wholesome from harmful substances.

Jacobson believed it to be an organ of secretion; Kölliker, that it secretes substances which have an influence on the specific nerves and enables the organism to be aware of the constitution of its own secretions.

Parker (1922) quotes Henning; the function of Jacobson's organ has to do with water-olfaction as contrasted with air-olfaction.

Klein (1880) says it is an accessory organ of smell especially as it is so well developed in animals and absent or rudimentary in man. Animals possess the sense of smell to such a degree that humans can hardly have a true conception of its nature, and Pearlman says Jacobson's organ is used by animals in "tracking" by smell.

As the organ is supplied by the same sensory nerve, the terminal nerve, which supplies the organ of smell in fishes, Broman is of opinion that the vomeronasal organ is the old water-organ of smell of the vertebrates adapted for terrestrial life.

Experimental proofs.—The contents can be expelled from Jacobson's organ in a freshly killed calf by pressure of the finger from behind forwards when under water.

Hamlin (1930) injected stain into the nose during life and killed the animal immediately, but found no colour in Jacobson's organ. He proves that blood-pressure is the agent for emptying Jacobson's organ. He further shows that air and liquid are forced out of Jacobson's organ by increasing the blood-pressure by means of adrenalin, and conversely that liquid is drawn into Jacobson's organ when the blood-pressure falls following the disappearance of the effects of adrenalin.

Teydel found glandular secretions in the cavity of the organ, never air, and believes that it is only by the presence of this liquid that perception takes place; Broman (1927) proved by morphological and experimental researches that the organ always contains a serous fluid which can be sucked from the nasal or oral cavity and that some mechanism

From above.—When viewed from above it was seen that the organ lies above the incisive canal—one-third of the organ anterior to the canal and two-thirds posterior.

Monkeys (Rhesus).—Four specimens were dissected—two young and two older specimens.

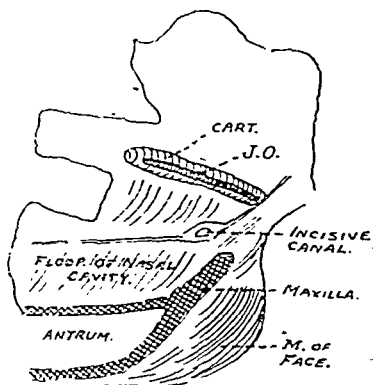


FIG. 1.

FIG. 1.—Human. From above (nasal septum bent slightly away from centre) showing Jacobson's organ.

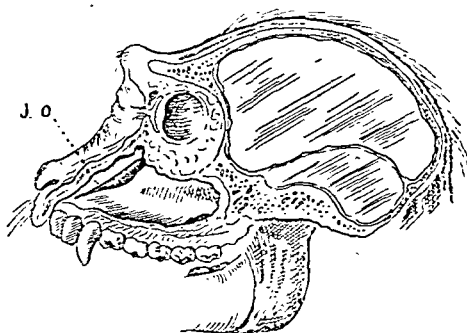


FIG. 2.

FIG. 2.—Monkey (rhesus). Showing Jacobson's organ.

In an adult specimen Jacobson's organ was found on both sides. The organ is placed high up on the lateral surface of the septal cartilage. It is pear-shaped, higher up the septum than in man, and lies at approximately an angle of 30° to the floor of the nose. It is noteworthy that the organ is placed so high as compared with humans and other animals. In all specimens each Jacobson's organ opened by a single orifice just within the anterior nares.

Sheep.—Nine specimens were dissected.

Jacobson's organ passes nearly horizontally to the soft palate to the floor of the nasal cavity through the anterior-lateral part of the incisive canal where the orifice of the organ opens; medially are the naso-palatine nerves and greater palatine artery.

Composition and constitution.—The organ lies in a fibrous cartilaginous tube about 0.5 cm. in external diameter; the internal diameter being about 2 mm.; mucous membrane lining shaped like a test tube with a concave upper border following the lower border of the premaxilla.

Size.—The length is usually described as from 2.5 to 4 cm. long and this was the case with all specimens dissected except one in which the length of the organ (including orifice) was 6 cm. with Jacobson's cartilage another 1 cm. in length.

Jacobson's cartilage lies within the shallow groove of the cartilaginous nasal septum with a thin layer of fibrous tissue between: it covers Jacobson's organ from end to end, being somewhat thicker at its lower surface and accompanies the orifice of the organ to its opening, completely surrounding and protecting it, just within the incisive canal.

Pig (seven specimens).—Jacobson's organ lies parallel to the floor of the nose and the palate and runs forward to the incisive canal where it opens a short distance within the

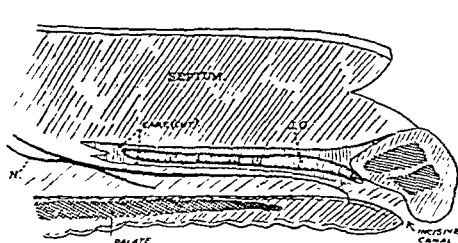


FIG. 3.

FIG. 3.—Sheep. Showing orifice of Jacobson's organ high up in incisive canal.

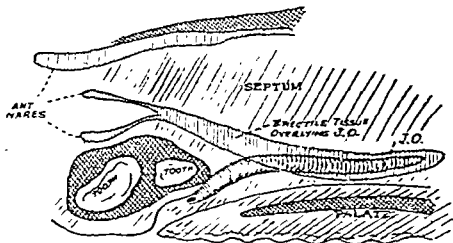


FIG. 4.

FIG. 4.—Pig. Showing relationship to incisive canal.

collection, of the nose of a newborn child prepared by Mr. Shattock to show the normal development of Jacobson's organ.

Noyes (1934) found Jacobson's organ present in ten newborn infants; Kölliker and others have shown that it is always present in the foetus, often in young children, and occasionally in adult man.

The organ nearly disappears in the higher mammals, and what is left of Jacobson's organ in man, enters into the formation of the incisive canal (Neal and Rand).

There has been some controversy as to whether the structure seen in man, in various stages of development, is, in fact, the same anatomical entity as that found in the same region in many animals; this is quite understandable in view of the varied anatomical arrangements already mentioned, and discussed under heading "Comparative".

According to Gegenbaur, the organ of Jacobson has not yet been demonstrated in man (Franke, 1921) but Wiedersheim believes that the progenitors of man must have possessed an organ of Jacobson, since the existence of Jacobson's cartilage is evidence that they did so (Franke). This is now the generally accepted opinion.

Pathological importance.—As is the case with other vestigial remnants, Jacobson's organ is occasionally the site of pathological changes. Corning states that, in man, degeneration of Jacobson's organ commences during the fourth month of life. Kölliker (see Franke) is of the opinion that the lumen of the organ may be obliterated by excessive epithelial growth and that calcareous material may be deposited in its walls.

L. Browne (1899) says that Jacobson's organ predisposes to inflammation as it is a blind sac and favours accumulation of bacteria. Jacobson's organ is of clinical interest as it corresponds with the seat of certain morbid changes: perforating ulcers and neuritic lesions, as seen in lupus, typhoid, leprosy and typhus.

Peter (see Franke) expresses the view that its disappearance in childhood is a result of the multiple inflammations which occurs in the nasal cavity.

It is also stated that exostoses of the nasal septum are due to hypertrophy of Jacobson's organ; such exostoses occur only in this region, but although Jacobson's organ is large and active in childhood, exostoses of this type occur only in adults; on the contrary, Onodi, suggests that they are due to Jacobson's cartilage; he is supported by Franke (1921) who suggests that thickening of the septum in this area may be due to a thickening of the spur of the septal cartilage at the edge of the vomer (which is closely associated with Jacobson's cartilage). Mihalcovics concludes that the organ can only be considered as a rudiment when present, and not as a defect when it is absent (Denker and Kahler, 1925).

The present writer (with Brandt, 1940) described a cyst in the posterior portion of Jacobson's organ in a human foetus of 124 mm. (80 mm. c.r.l.). As this part of Jacobson's organ lies above the nasal opening of the incisive canal it is possible that increase in size of the cyst might be downward into the lumen of the canal and cause a cyst of the latter. This is one of the suggested explanations of cysts in this region.

INVESTIGATIONS

During the investigation which preceded the writing of this paper dissections were made as follows:

Human, 3 (Jacobson's organ found in one).

Monkeys, 4; sheep, 9; pigs, 7; cows, 5; calves, 4 (Jacobson's organ found in all).

The writer acknowledges the fact that strictly scientifically these specimens are listed in the reverse order, but the importance of the findings in man and monkey appears to justify this departure for the special purpose of this paper.

Human.—Twenty adult specimens were examined (visually only) for Jacobson's organ without success. Three specimens were dissected thoroughly with the result that Jacobson's organ was found in one specimen.

Human specimen No. 3.—Jacobson's organ and cartilage were present and incisive canal was patent.

Description.—This specimen shows bilateral Jacobson's organ, neither of which was patent nor could an ostium be found; both Jacobson's organs were covered by well-defined cartilage 1 cm. in length; length of the organ was 0.8 cm., width was 0.2 cm.; Jacobson's organ was firmly attached to the mucous membrane anteriorly; the relationship to the incisive canal is shown in diagrams. The impression gained was that a cyst of Jacobson's organ could not easily bulge into the canal.

The centre of Jacobson's organ is 1 cm. above the nasal orifice of the incisive canal, and the blood-vessels pass beneath it.

Laterally.—On removing the mucous membrane of the nasal septum about 1 cm. above the floor of the nose a small elongated cartilaginous mass was found lying antero-posteriorly practically parallel with the palate.

From above.—When viewed from above it was seen that the organ lies above the incisive canal—one-third of the organ anterior to the canal and two-thirds posterior.

Monkeys (*Rhesus*).—Four specimens were dissected—two young and two older specimens.

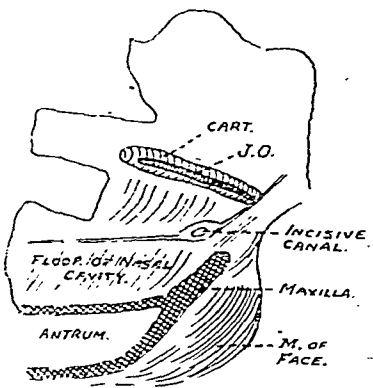


FIG. 1.

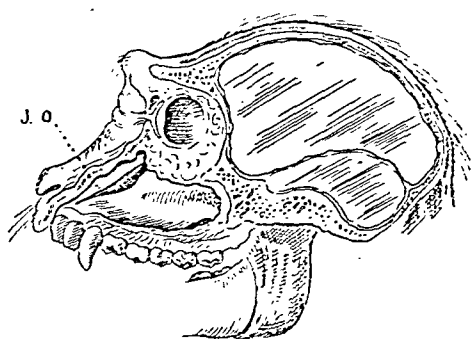


FIG. 2.

FIG. 1.—Human. From above (nasal septum bent slightly away from centre) showing Jacobson's organ.
FIG. 2.—Monkey (*rhesus*). Showing Jacobson's organ.

In an adult specimen Jacobson's organ was found on both sides. The organ is placed high up on the lateral surface of the septal cartilage. It is pear-shaped, higher up the septum than in man, and lies at approximately an angle of 30° to the floor of the nose. It is noteworthy that the organ is placed so high as compared with humans and other animals. In all specimens each Jacobson's organ opened by a single orifice just within the anterior nares.

Sheep.—Nine specimens were dissected.

Jacobson's organ passes nearly horizontally to the soft palate to the floor of the nasal cavity through the anterior-lateral part of the incisive canal where the orifice of the organ opens; medially are the naso-palatine nerves and greater palatine artery.

Composition and constitution.—The organ lies in a fibrous cartilaginous tube about 0.5 cm. in external diameter; the internal diameter being about 2 mm.; mucous membrane lining shaped like a test tube with a concave upper border following the lower border of the premaxilla.

Size.—The length is usually described as from 2.5 to 4 cm. long and this was the case with all specimens dissected except one in which the length of the organ (including orifice) was 6 cm. with Jacobson's cartilage another 1 cm. in length.

Jacobson's cartilage lies within the shallow groove of the cartilaginous nasal septum with a thin layer of fibrous tissue between; it covers Jacobson's organ from end to end, being somewhat thicker at its lower surface and accompanies the orifice of the organ to its opening, completely surrounding and protecting it, just within the incisive canal.

Pig (seven specimens).—Jacobson's organ lies parallel to the floor of the nose and the palate and runs forward to the incisive canal where it opens a short distance within the

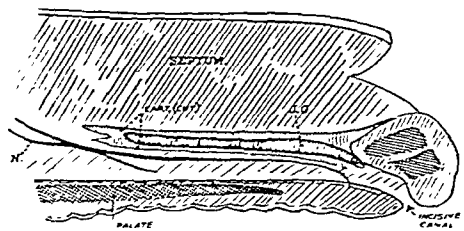


FIG. 3.

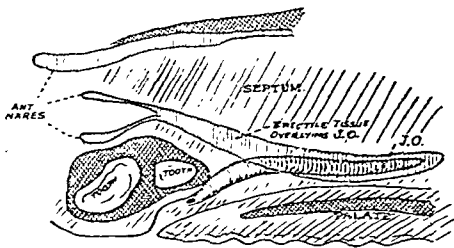


FIG. 4.

FIG. 3.—Sheep. Showing orifice of Jacobson's organ high up in incisive canal.
FIG. 4.—Pig. Showing relationship to incisive canal.

canal with a small rounded tube-like opening in approximately the same plane as that of the organ.

Jacobson's cartilage covers it completely above and within the canal, anteriorly there is a layer of "erectile" tissue at the region where the organ enters the canal.

At its anterior end Jacobson's cartilage becomes attached to the septal cartilage which flows with it within the incisive canal to the orifice of the organ, i.e. cartilage surrounds the organ to its orifice. The organ and its cartilage lie free at its posterior end—merely lying in a groove at the lower part of the nasal septum.

The anterior orifice of the organ lies at the level of the middle of the second incisor tooth, at a distance above the palatal orifice of the incisive canal. The canal is similar in angle and layout to that of the sheep.

Size of the organ: *Old pig*.—Length of organ 5 cm. Cartilage is 1 cm. longer. Organ is 2 to 3 mm. at widest. *Young pig*.—Length of organ 3.5 cm. Cartilage is 0.5 cm. longer. Organ is 2 to 3 mm. at widest.

Relationship within the incisive canal: Jacobson's organ lateral, blood-vessels medial.

Cow and calf.—Laterally Jacobson's organ is a lengthy structure about 9 cm. long and 1 cm. wide, lying roughly horizontal and parallel with the palate.

The anterior portion of the organ passes within the incisive canal to the under surface of the bony palate in the same plane as the organ and then turns abruptly inwards and forwards within the thickness of the fibrous covering of the anterior portion of the palate where the incisive canal opens at the papilla palatina on either side.

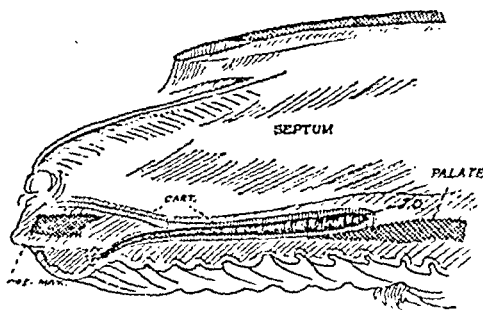


FIG. 5.—Cow. Dissection showing body and orifice of Jacobson's organ, anterior portion of palate cut away at an angle.

The anterior orifice of Jacobson's organ opens as a narrow slit just before the incisive canal opens on the palate; it is therefore necessary to dissect obliquely across the thickness of the palate to see the anterior portion of Jacobson's organ.

Jacobson's cartilage completely surrounds the organ and advances with it within the incisive canal as far as the opening of the organ. It is quite tightly apposed to the lower border of the cartilaginous nasal septum and appears to be closely attached thereto; careful dissection, however, shows that there is a thin layer of fibrous tissue intervening. Thus the relationship, as viewed from behind, is centrally the cartilaginous nasal septum, then a layer of fibrous tissue—thin at upper region and thicker below—then Jacobson's organ (oval in section) completely surrounded by Jacobson's cartilage which is thicker below. Finally and laterally a thick layer of mucous membrane which is the mucous membrane of the septum and is continuous over the nasal floor—a prolongation sweeps as a tube into the incisive canal as previously described.

Contents of the incisive canal.—There is a small artery posteriorly, then nerve and a larger artery, and then Jacobson's organ anteriorly, the arrangement within the canal from without in being—Jacobson's organ, nerve and artery.

Calf.—The organ is nearly as long and as wide as in adult cow. It is interesting to see in calf that Jacobson's cartilage is not adjacent to the side of nasal septal cartilage, but is suspended immediately below it by a fibrous ligament running the full length of the organ. Anteriorly, however, the cartilage becomes more firmly attached.

Cow, sheep and pig.—The incisive canal is very wide from front to back—narrow from side to side and runs at an angle of about 30 degrees from front to back, so that the premaxilla finishes, anteriorly to the canal, at an acute angle and the palate commences posteriorly also very sharply. The effect of the incisive canal is that of a sweep forwards and downwards of the mucous membrane into a narrow elongated tunnel opening by means of a very small orifice at the papilla palatina.

Human Embryos Examined

Human specimens of the following crown rump lengths were examined in serial section.—12.5, 32, 35 (sagittal), 35, 37, 70, 80, 124 mm. (eight in all); seven in frontal section and one in sagittal section.



FIG. 6.

FIG. 6.—Human embryo (frontal section). 12.5 mm. c.r.l. Showing Jacobson's organ just forming on left and lumen fully formed on right. Note absence of Jacobson's cartilage. $\times 46$.



FIG. 7.

FIG. 7.—Human embryo (sagittal section). 35 mm. c.r.l. Showing Jacobson's organ in full. Anterior orifice to left. $\times 46$.

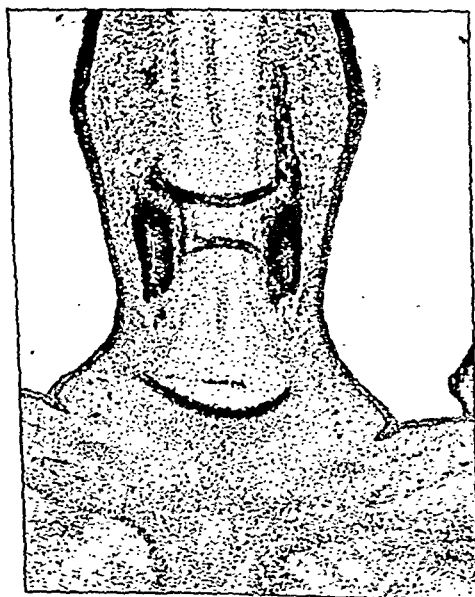


FIG. 8.



FIG. 9.

FIG. 8.—Human embryo frontal section). 37 mm. c.r.l. Showing lumen of Jacobson's organ. Note Jacobson's cartilage just beginning. $\times 59$.

FIG. 9.—Human embryo (frontal section) 70 mm. c.r.l. Beginning of Jacobson's organ. Jacobson's cartilages well shown. $\times 48$.

Embryo 12.5 mm. c.r.l.—Jacobson's organ lies in its usual position and begins 600μ from the tip of the embryo (nose). It consists of three definite portions: (a) a furrow in the mucous membrane 100μ long; (b) a tubular opening 20μ long; (c) a body 100μ long. Total length 220μ .

In this specimen the "tail", i.e. posterior tapering end, is very short.

There is no septal cartilage or Jacobson's cartilage in this specimen. There is no trace of the tooth band, which confirms Meyer's (Churchill) statement that this structure does not appear until 13 mm. stage.

Embryo 35 mm. c.r.l.—It is fortunately possible to study the embryology of the organ in embryos of this length—both frontally and sagittally.

Jacobson's organ frontally.—The first invagination of Jacobson's organ begins as a furrow in the edge of nasal mucous membrane for three sections and then a fine tube within the mucous membrane for three sections, opening at 2.4.10 into the body.

Length of Jacobson's organ in this specimen is furrow 30μ , tube 30μ , body 350μ , tail 140μ . Total length 550μ .

Jacobson's cartilage in its total length is 870μ . It is 320μ longer than Jacobson's organ, appearing 50μ before and ending 270μ behind the "tail" of the organ.

Shape and description of Jacobson's cartilage.—The structure varies very much in shape throughout its length; in general it forms a complete protection to the lower aspect of Jacobson's organ. It is mainly free at its anterior end, but becomes closely apposed to the cartilage of the nasal septum posteriorly; at no time does Jacobson's cartilage become merged into the nasal septum; there is always a layer of tissue between—only one cell in thickness in much of its length.

It first appears as an isolated ovoid piece of cartilage below and some distance away from the septal cartilage.

It approximates the tip of the septal cartilage as an upright oblong cartilage at 3.1.9, 210μ later, and remains in close contact here, but varying in shape, oblong to triangular, "L" shaped, crescent shaped and ovoid again until section 4.1.12, i.e. 510μ in length, when it is again separate from the septal cartilage as a small ovoid cartilage and disappears at section 4.3.2; so that the relationship of Jacobson's cartilage to the septal cartilage is: Anterior portion free of septal cartilage 210μ ; middle portion in contact with septal cartilage 510μ ; posterior portion free of septal cartilage 150μ .

Relationship to incisor teeth.—The first incisor tooth first arises at 2.2.4 and ends at 2.3.10 where the tooth band immediately gives rise to the second incisor, i.e. 70μ before the beginning of Jacobson's organ and practically the same level as beginning of Jacobson's cartilage.

Embryo 35 mm. Cut in sagittal section.—Crown rump length $35,000\mu$; width of head $6,500\mu$; width of nasal cavity proper one side 550μ . There is, in addition, a narrow prolongation of the nasal cavity outwards of 130μ (? antrum or other sinus); total width of nasal septum 370μ ; width of Jacobson's organ at its widest (one side) 80μ ; width of Jacobson's organ at its widest (other side) 90μ . From this measurement it will be seen that the two Jacobson's organs occupy approximately one-half of the width of the septum. Total length of organ is 550μ .

Jacobson's cartilage is a total width of 120μ and lies underneath Jacobson's organ overlapping both sides of the organ about 10μ or 20μ . In shape longitudinally it varies from nearly round, through crescent shape to club shape, when in the middle of its width and at its posterior end it becomes closely apposed to the cartilaginous septum. Length of cartilage is 870μ .

Relationship to the incisor teeth.—The whole of the organ, including its orifice, is just behind the forming second incisor.

Embryo 37 mm. c.r.l. Frontally.—Jacobson's organ begins at 121 sections ($1,210\mu$) from tip of nose. Jacobson's organ is present in 37 sections = length 370μ and Jacobson's cartilage is 570μ .

This specimen is interesting because Jacobson's cartilage begins 100μ behind the first invagination of Jacobson's organ.

Size of organ invagination, furrow and tubular entrance 90μ ; body 250μ ; tail 30μ .

In this specimen Jacobson's organ begins and ends at the same levels on both sides. In the other specimens examined, Jacobson's organ is not symmetrical, but begins and ends several μ later on one side than the other.

Jacobson's cartilage shows much the same course and variations in size as in the 35 mm. specimen described above; it is first attached to the septal cartilage at its commencement and becomes free at section 5.2.8, i.e. there is a posterior unattached portion of Jacobson's cartilage of 70μ , i.e. length of Jacobson's cartilage = 570μ .

Relationship to incisor teeth.—The first invagination of Jacobson's organ coincides with the first heaping up of epithelium of the tooth band in the formation of the first incisor tooth and its "tail" terminates just at the plane where the epithelium is heaping up to form the primordium of the second incisor, i.e. rather more forward than in the others described.

Embryo 70 mm. c.r.l.—In this specimen both Jacobson's organs begin at section 8.1.3; one ends at 9.4.3; i.e. length (a) 650μ , (b) 750μ .

Jacobson's cartilage begins at section 5.3.1 as small outgrowths laterally at the tip of the nasal septum (i.e. a small separate anterior portion of 80μ) at 5.4.1 the outgrowths become isolated, slightly smaller, then nearly horizontal—split into smaller portions and after changes in shape similar to those dissected in the 35 mm. specimen; the cartilage becomes closely apposed to the septal cartilage at 8.1.1, i.e. just before first invagination of Jacobson's organ and settles down to a long thin downward projection of cartilage curving slightly outward at its lower end. Unfortunately the specimen ends at section 10.6.6 and as the cartilage is still present there, no length can be given for it.

Relationship to incisor teeth.—The first incisor tooth germ ends and second begins at 7.4.1. The latter is well shaped at section 8.1.3 where Jacobson's organ commences (this is about half-way through the tooth germ); at section 8.4.5 the shape of the second incisor is just ended and the tooth band is continuing towards the canine tooth.

SUMMARY OF EMBRYOLOGICAL INVESTIGATIONS

Jacobson's organ is found in its typical arrangement in all of eight human embryos examined; Jacobson's cartilage is present as a protective covering in all except the smallest (12.5 mm.).

The organ is relatively large in the 12.5 mm. specimen and is of diminishing size, relatively, as the size of the embryo increases.

There is no constant relationship between length of embryo—length of Jacobson's organ—length of Jacobson's cartilage—position of Jacobson's organ *vis-à-vis* Jacobson's cartilage, and to position of developing incisor teeth.

Sizes.—In 12.5 mm. specimen Jacobson's organ is 220μ long; 35 mm. specimen Jacobson's organ is 550μ long; 37 mm. specimen Jacobson's organ is 370μ long; 70 mm. specimen Jacobson's organ is (a) 650μ long, (b) 750μ long.

In 12.5 mm. specimen Jacobson's cartilage is not present; 35 mm. specimen Jacobson's cartilage is 870μ long; 37 mm. specimen Jacobson's cartilage is 570μ long; 70 mm. specimen Jacobson's cartilage is $1,950\mu$ present on the slides + an unknown further length.

DISCUSSION

It is rather remarkable as a result of study of the literature to find that many anatomists and embryologists confuse the incisive canal with the tubular part of Jacobson's organ, thus clouding the fact that there are two general patterns of Jacobson's organ: (a) As in human—opening in anterior nares (i.e. remote from the incisive canal); (b) as in most mammals—opening within Stenson's canal (i.e. within the incisive canal).

A similar misunderstanding occurs in regard to the association of Jacobson's organ with Jacobson's cartilage; there appear to have been three general views: (a) Jacobson's organ and Jacobson's cartilage are the same structure; (b) Jacobson's organ is associated with and protected by Jacobson's cartilage; (c) that the two structures are quite unrelated.

In spite of these contrary views the general view among embryologists is that the close and intimate association with a protecting cartilage is evidence that the organ is Jacobson's organ. Possession of Jacobson's cartilage may be taken as confirming the presence or previous existence of Jacobson's organ, as the cartilage is developed merely as a protection to the organ.

In calf, dissection shows Jacobson's cartilage to be in the same dependent position as is the case in human embryos.

As to the opening of the anterior orifice of the organ there can be no doubt that in some animals the organ opens anteriorly remote from the incisive canal; nevertheless, it is apparent that the typical animal has the duct opening within the incisive canal.

The statement by Watson-Williams is confirmed. It is not usually possible to see Jacobson's organ in human adults, and only by a careful dissection is an occasional one found.

It must be granted that Jacobson's organ, even in humans, had some original importance—Franke quotes Keibel finding the organ in an embryo of 8 mm. and Peter in one of 9.2 mm., and the present writer shows it extremely well developed in one of 12.5 mm.

In adult humans the length as described by various authors is from 2.28 to 8.43 mm.—a human specimen is described possessing Jacobson's organ of 8 mm. length. Franke describes the organ as being about 1 cm. above the floor of the nose, Kölliker 8.5 mm. In the specimen described in this paper the distance was 1 cm.

The interior of the organ is highly specialized, with columnar cells on the innermost layer (i.e. lining the lumen of the organ) and a glandular type of epithelium on the medial aspect of its cavity.

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There is no septal cartilage or Jacobson's cartilage in this specimen. There is no trace of the tooth band, which confirms Meyer's (Churchill) statement that this structure does not appear until 13 mm. stage.

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Section for the Study of Disease in Children

President—HELEN M. M. MACKAY, M.D., F.R.C.P.

[October 27, 1944]

DISCUSSION ON NUTRITION OF THE PREMATURE INFANT IN THE FIRST MONTH OF LIFE

Dr. Helen M. M. Mackay: Many writers have drawn attention to two facts: that our neonatal mortality compares unfavourably with that in some great European cities before the war, and that half or more of the babies who die in the first four weeks of life are premature or immature (McNeil, 1940; Baird and Wyper, 1941; Parsons, 1944).

Until recently in this country the care and feeding of premature babies have been almost entirely in the hands of midwives. Experienced maternity ward sisters have had very good results, but there has been no systematic teaching on the subject of feeding, and each midwife, and, indeed, each pædiatrician, has had to learn at the expense of the infants. Though I am certain that neonatal mortality could be reduced by a better knowledge of how to feed premature babies, this is but one aspect of an intricate problem. Good results with these frail infants cannot be obtained in any hospital without certain essentials: highly skilled and devoted nursing, a sufficient number of nurses, rigid care in the prevention of cross infection and the maintenance of the baby's normal body temperature, and also good midwifery. It is a great advantage in maternity hospitals to appoint special baby nurses responsible for infant feeding so that the babies' routine is not upset by any obstetric emergencies which claim the whole attention of the midwives on duty. The credit for the successful rearing of a small premature infant belongs primarily to the nurse in charge; but she needs skilled medical advice and help. While on the subject of general care, I should like to stress the importance of body temperature in relation to feeding. A baby is much more likely to swallow and to suck if his temperature is between 98° and 100° than if it is between 96° and 98°; a cold baby will not take his food and chilling is a common cause of lack of vitality, of atelectasis and of consequent cyanotic attacks. I believe œdema in the premature baby is usually an indication of previous chilling, and its significance is often missed. I can offer no evidence as to whether ascorbic acid influences the stability of body temperature, as Levine and his co-workers (1941) think possible.

Perhaps the best approach to the problem of how to feed premature babies in the neonatal period is to consider first the normal food of normal babies (Mackay, 1941a). The values given in Table I (which was compiled from many estimations by three different groups of workers), show that, for colostrum and early milk combined in the first two

TABLE I.—COLOSTRUM AND EARLY BREAST MILK: COMPOSITION AND CALORIE VALUE.
(Figures in brackets represent number of samples on which the mean value is based.)

Period after parturition	Protein %	Sugar %	Fat %	Calories per fluid ounce	Authors
1st day	7.86 (11)	3.17 (14)	—	—	Widdows <i>et al.</i> 1935
5th day	1.70 (20)	6.94 (28)	—	—	Ditto
8th—13th day	1.45 (26)	6.35 (46)	4.34 (11)	20.7 (11—46)	Widdows <i>et al.</i> 1930 and 1933
1st—13th day	2.39(108)	5.84(115)	3.53 (24)	18.9 (24—115)	Ditto
5th day	1.74 (8)	6.08 (8)	2.88 (8)	17.3 (8)	Hammett, 1917
3rd—11th day	2.00 (40)	6.09 (40)	3.02 (40)	18.9 (40)	Ditto
3rd—12th day	2.25 (5)	7.59 (5)	3.13 (5)	18.7 (5)	Holt <i>et al.</i> , 1915
1—9 months	1.15 (17)	7.50 (17)	3.26 (17)	18.4 (17)	Ditto

weeks after delivery, the mean figures for protein, carbohydrate, fat and calorie value are very similar to those for mature breast milk, except that the protein value is higher—namely 2%, or a little over—in the secretion of the first two weeks. The mean protein value for this period is raised by the very high protein content of the scanty secretion of the first few days, but as early as the fifth day, the protein content of the breast secretion is only about 1.7%. The mean calorie value for the first two weeks is about 19 per fluid ounce. This is almost exactly the mean value found by various workers for mature milk. Nature, therefore, does not provide the newborn baby with a dilute food, a fact worth bearing in mind. Since the calorie value of mature breast milk is usually reckoned in round figures as 20 per fluid ounce, I have adopted this figure when calculating the baby's intake during the first week.

One obvious method of ascertaining the calorie requirements of babies during the first

DEC.—DIS. IN CHILD. 1

of a typical Jacobson's organ and its position and structure can aid in the exact allocation of animals whose species is doubtful. Weber's statement that in mammals the anterior part of Jacobson's cartilage usually remains in contact with the septum, and appears to rise from the anterior part of the septum and to extend free backwards is confirmed in the case of pig.

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Babies weighing 2 and 3 lb. usually start with 12 feeds in the twenty-four hours, those weighing 4 lb. with 12 or 10 feeds, those weighing 5 lb. with 8 or 6 feeds in twenty-four hours. At 7 days old the 2-lb. baby is probably still having 12 feeds daily, whereas the

TABLE III.—MIXTURES AND SOLUTIONS CONTAINING APPROXIMATELY 20 CALORIES PER FLUID OZ.

Name	Foodstuff	Quantity	Water
Dried milk, full cream*	...	1 drachm or 1 level measure†	To 1 fl. oz.
‡ cream, unsweetened*	...	1½ " " 1½ " "	" 1 " "
‡ cream, sweetened*	...	1½ " " 1½ " " †	" 1 " "
Condensed milk, sweetened‡	...	1 fluid oz. or 1 level teaspoonful§	" 5 " "
Sugar, castor or granulated	...	1½ drachm or 1½ level teaspoons§	" 1 " "
lactose	...	1½ " " 2 " " §	" 1 " "

* Roller process dried milk should be freshly mixed for each feed.

† The measure should be that provided for the brand used.

‡ Condensed milk should be freshly diluted for each feed if a refrigerator is not available.

§ The teaspoon used should hold 1½ fluid drachms.

5-lb. baby will probably be getting only 6 feeds. After the first week of life further increases in the food are made, each increase being considered in the light of the baby's rate of gain in weight, his appetite, and his toleration of the quantity he is taking. Particular attention is paid to whether or not there is any abdominal distension or fullness. Most small premature babies need 60 calories or more per pound body-weight by the third week of life. In addition to his food, each baby is prescribed extra water. During the first few days the intake of water amounts, if possible, to as much again as the volume given in the feeds; by the end of the first week it is usually considerably less than the volume of the feeds. The nurse gives extra water after, during or between feeds according to how the baby takes it best. Babies who do not swallow, or swallow very slowly, are fed by catheter for some or all the feeds. The great majority of small premature babies, however, are spoon-fed at first, but all those who are able to suck are encouraged to take from a bottle or direct from the breast as soon as they can do this without being over-tired. The schedule is merely a guide, and every nurse must use her judgment at each individual feed as to how far it is wise to press the baby to take, and experience and good judgment are very necessary in this matter. Babies are most often fed propped up on the nurse's knee, but I do not attempt to lay down any general rule on the subject—some babies are fed in their cots. Each baby has a day-sheet on which the nurse keeps a full record of food and fluid taken, stools passed, body temperature and any symptoms.

Vitamin D, usually in the form of cod-liver oil emulsion, later changed to cod-liver oil compound, is given in small divided doses, as soon as the baby is established on his feeds, being started very gradually. Ascorbic acid is started next. Iron and ammonium citrate is often given before the baby goes home in order to simplify the mother's task, though I do not think extra iron is necessary until the baby is about 2 to 2½ months old. Before the war no premature baby was discharged unless (1) he was making good progress; (2) he was having not more than 6 feeds in twenty-four hours; (3) he was sucking from the breast if the mother had breast milk; (4) he was having supplements of vitamins A, D and C; (5) the mother had herself undertaken in the hospital the task of feeding him and making up any artificial feeds; and (6) home circumstances were such that satisfactory care of the baby was possible.

The following graphs show the ordinary progress of individual babies fed on the lines I have indicated.

A 4¼ lb. baby, shown in Chart 2, regained his birth-weight by 6 days old, although he did not take approximately 50 calories per pound body-weight until 8 days old. He was 10½ oz. over birth-weight by 2 weeks old. For his last week in hospital he was wholly fed at the breast. Chart 3 shows the progress of W. B. weighing 3 lb. 5 oz. at birth. The calorie intake was slightly lower than the formula requirement. He regained birth-weight by the 10th day, and by 4 weeks old was 19 oz. over birth-weight.

A baby of 2 lb. 9 oz., whose rate of growth is shown in Chart 4, took more than the schedule scale of nourishment. Œdema accounted in part for a very rapid increase in weight in the second week of life, but the œdema had disappeared by 14 days old, and by 4 weeks old he was 20 oz. over his birth-weight and beginning to suck from the breast. These three infants were selected at random, as already stated, in order to show the type of gain obtained with this system of feeding.

Premature babies born in the Mothers' Hospital show a higher hæmoglobin level by about 2 to 3 months of age than do many premature babies (Mackay, 1935). Whether or not this is due to this type of feeding I do not know.

Our neonatal mortality at the Mothers' Hospital is considerably higher now than it was before the war, but as the system of feeding has remained the same, this must be attributed to other factors. In the year before the war (June 1938 to June 1939), among

ten days of life is to consider the intake of normal newborn babies who are wholly breast-fed and are making good progress. Since small premature babies cannot take their full requirement from the breast, let us consider the intake of bigger babies. In order to obtain the necessary data, I calculated the intake of a consecutive series of 20 babies born at the Mothers' Hospital who were wholly breast-fed. These babies weighed between 5 and 10 lb. at birth. Chart 1 shows the intake of ten babies in this series who, at 10 days old, exceeded their birth-weight. These babies averaged 7 lb. in weight at birth. I assumed that each day's intake had a mean caloric value of 20 per fluid ounce, but this figure may be too low for the first two to three days. In any case the caloric intake goes up-step by step each day, and by the seventh day of life has reached nearly 50 calories per pound body-weight at birth. I compared the intake of these babies with the quantity of milk they would have received if fed according to a formula which I have now used for a good many years as a guide in feeding hand-fed infants of all sizes during the first week of life (Mackay, 1941a). According to this formula I aim at giving hand-fed babies 50 calories per pound birth-weight on the seventh day of life. One-seventh of 50 calories per pound body-weight is given on the first day, increasing by the same amount each day, so that by the seventh day the baby is taking 50 calories per pound birth-weight. During the first two days, when breast secretion was scanty, these normal babies took considerably less than the formula prescribes, as one would expect, but thereafter the intake increased steadily (Chart 1). The total intake of the group is shown in Table II. From 2 to 7 days old, the total intake tallied almost exactly with

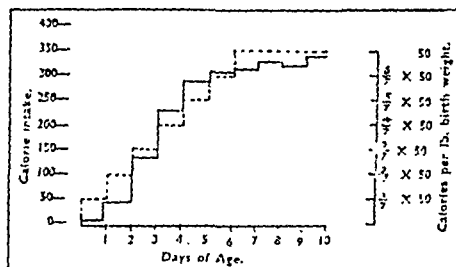


CHART 1.—Calorie requirements of first week of life (Mackay, 1941).

..... Mean caloric intake of 10 babies who at 10 days old exceeded their birth-weight; mean birth-weight 7 lb.
 Caloric requirements by formula.

TABLE II.—CALORIE INTAKE IN THE FIRST EIGHT DAYS OF LIFE OF 20 CONSECUTIVE BREAST-FED BABIES AT THE MOTHERS' HOSPITAL.

Weight at 10 days	No.	Mean b.-wt. lb. oz.	Wt. in relation to b.-wt.		Intake as per cent. of formula fig. for 2-7 days
			At 7 days oz.	At 10 days oz.	
Over birth-weight	10	6 15½	+ 1.3	+ 3.65	101
At birth-weight	4	6 16½	- 1.7	+ 0	93
Under birth-weight	6	6 11½	- 5.25	- 3.0	72

that of the formula (it exceeded it by 1%). I constantly use the formula as a yard stick against which to check the intake between the 2nd and 7th day of life of breast-fed babies who fail to make good progress, and have found it very useful, though it sometimes happens that an individual baby, making good progress, may take much more or much less, in ounces, than the formula provides, possibly because his mother's milk differs from the average in caloric value. In this same series of 20 babies there were 4 babies who just reached birth-weight by 10 days old, and 6 babies who failed to reach birth-weight by that age. Their mean intake for the period from 2 to 7 days old was 93% and 72% respectively of the caloric intake indicated by this formula (see Table II).

Opinions vary as to the nature of the food to be given to newborn premature babies. I have had satisfactory results with breast milk, and, whenever possible, use this during the first few days after birth. In a maternity hospital breast milk is nearly always obtainable for the very small babies. I do not add protein to breast milk as some clinicians advocate. Failing breast milk, I generally use either sweetened half-cream dried milk, or sweetened condensed milk, but these are not as well tolerated. The quantity of food given is, I think, much more important than the balance between protein, fat and carbohydrate in different types of artificial food in use for newborn infants.

At the Mothers' Hospital, all feeds are ordered in a concentration to provide 20 calories per fluid ounce. Each ward is provided with a typed schedule of feeding for premature babies of different birth-weights, calculated from the formula I have given you (Mackay, 1941b). A second schedule (Table III) shows how to prepare dried milk and condensed milk in a dilution to provide 20 calories per fluid ounce (Mackay, 1941b). Feeding is generally started about six hours after birth in the hope of minimizing the initial loss in weight.

in three out of the five years the mortality was slightly lower than it was in the year I have myself analysed. All these figures apply to the period spent in hospital, but even so, compare very favourably with the Registrar-General's mortality figures for the first

TABLE IV.—CALORIE INTAKE OF PREMATURE BABIES IN THE FIRST TWO WEEKS OF LIFE.

Age in days	No. of babies	Calorie intake per day		Calories required by formula scale	
		Total	Per lb. b.-wt.		
0	43	12 (12 hrs.)	3	7	
1	"	52	11	14	
2	"	85	18	21	
3	"	125	27	28	
4	"	158	34	35	
5	"	179	39	42	
6	"	205	44	50	
7-14	26	228	53	—	
Mean b.-wt. lb. oz.	Max. loss 1st week (mean) oz.	1st week (mean) per cent. b.-wt.	Difference from b.-wt.		Gain in 2nd week oz.
4 10	3.8	5.1	At 7 days oz.	At 10 days oz.	5.4
			- 1.7	+ 0.4	

28 days of life: namely 28.3 per 1,000 live births in England and Wales in 1938, or 2.83% (Stocks, 1944).

I am indebted to the co-operation of the nursing staff and the resident medical staff of the Mothers' Hospital for these detailed records.

Standardization of routine infant feeding in a hospital is of great value as it enables all nurses and house officers to become thoroughly familiar with its details, and reduces to a minimum the likelihood of gross errors or of sudden unintentional changes in feeding through changes in the baby's nurses or medical attendant.

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If breast milk cannot be obtained, cow's milk will have to be used, and as it is less digestible, tolerance must be established by giving small quantities of weak feeds in gradually increasing amounts.

The premature baby has difficulty in digesting both the protein and fat of cow's milk. Approximately 2.0% protein can be given by the age of 2 weeks, if the curd is modified by dilution, boiling, condensation, drying, lactification or peptonization; but few premature babies can digest more than 1.5% to 2.0% of fat by this age. Sugar is well tolerated, especially cane sugar. Suitable artificial feeds are therefore: (1) Sweetened condensed milk (1 in 16 to 1 in 6). (2) Unsweetened condensed milk, with 1 drachm of cane sugar to 3 oz. of mixture (1 in 12 to 1 in 4). (3) Full-cream dried milk with 1 drachm of cane sugar to 2 oz. of mixture (1 in 32 to 1 in 16). (4) Peptonized or lactified cow's milk with 1 drachm of cane sugar to 2 oz. of mixture (1 in 4 to 1 in 2).

Half-cream dried milk, diluted to reduce the protein to a suitable level, contains too little fat for the healthy premature baby, while humanized dried milk contains too high a percentage of fat. Undiluted whey should not be given, owing to the high percentage of mineral salts (0.65%) and the danger of salt retention and oedema.

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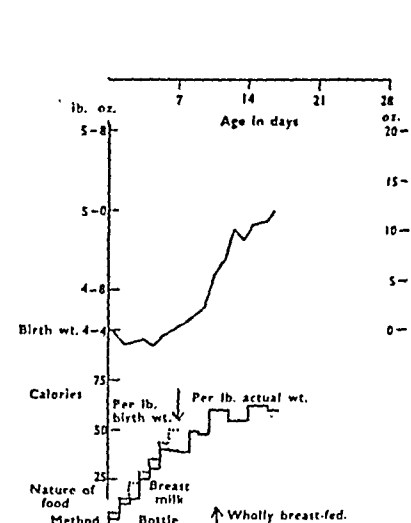


CHART 2.—B., born 1.7.43 (Mothers' Hospital).

The calorie requirements by formula are indicated by the dotted line. The calorie intake is indicated by the continuous line

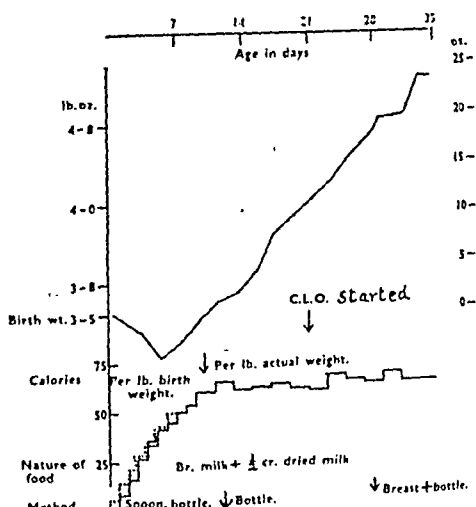


CHART 3.—W. B., born 15.10.43 (Mothers' Hospital).

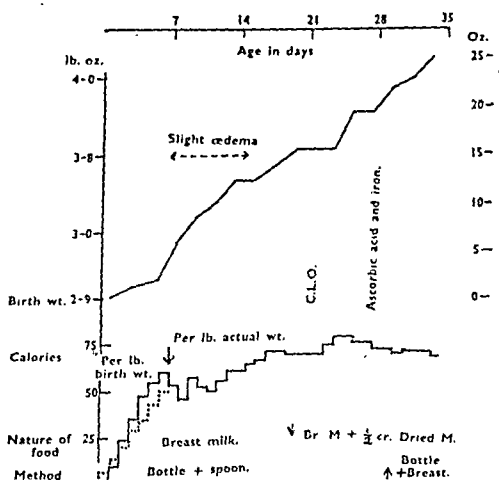


CHART 4.—B. P., born 24.7.43 (Mothers' Hospital).

The calorie requirements by formula are indicated by the dotted line. The calorie intake is indicated by the continuous line.

118 premature babies, there were 12 deaths, i.e. a mortality of 10%. One of the 12 deaths occurred at 34 days of age of pneumonia, that is after the ordinarily accepted neonatal period. Of the remaining 11 infants, one died as the result of exomphalos, and 10 died within 36 hours of birth with failure to establish normal respiration. I think I can safely say that in no case was the method of feeding a factor in the cause of death. The 107 babies surviving at 10 days old showed a mean loss in weight after birth of 3.6 oz., that is 4.6% of their birth-weight, and at 10 days old they averaged 1 oz. over birth-weight. Full details are available of the feeding of 43 of these babies, including nearly all the smallest, until 10 days old (Table IV). Their mean calorie intake for the first 10 days of life was 94% of the formula allowance, their mean intake on each of the first 7 days being slightly lower than the formula scale. Their initial loss in weight was 5% of their birth-weight, and at 10 days their mean weight was half an ounce over birth-weight. In the second week of life their mean intake was 53 calories per pound body-weight, and the mean gain $5\frac{1}{2}$ oz. 1938-39 was not selected as an especially favourable year. I analysed the total mortality among all babies, full term and premature, born alive in the hospital that year and found it to be 1.3%. The total infant mortality rate, according to the Hospital Registrar's figures, for the five years 1932-36 inclusive was: 1.2, 2.3, 1.2, 1.1 and 1.8% respectively; that is

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Mean b.-wt. lb. oz.	Max. loss 1st week (mean) oz.	Difference from b.-wt.		Gain in	
4 10	3.8	At 7 days	At 10 days	2nd week	
	per cent. b.-wt. 5.1	oz. — 1.7	oz. + 0.4	oz. + 5.4	

28 days of life: namely 28.3 per 1,000 live births in England and Wales in 1938, or 2.83% (Stocks, 1944).

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Food.—Breast milk is generally accepted as being the best food for the premature baby. It may be given diluted during the early days, if the baby is small.

If breast milk cannot be obtained, cow's milk will have to be used, and as it is less digestible, tolerance must be established by giving small quantities of weak feeds in gradually increasing amounts.

The premature baby has difficulty in digesting both the protein and fat of cow's milk. Approximately 2.0% protein can be given by the age of 2 weeks, if the curd is modified by dilution, boiling, condensation, drying, lactification or peptonization; but few premature babies can digest more than 1.5% to 2.0% of fat by this age. Sugar is well tolerated, especially cane sugar. Suitable artificial feeds are therefore: (1) Sweetened condensed milk (1 in 16 to 1 in 6). (2) Unsweetened condensed milk, with 1 drachm of cane sugar to 3 oz. of mixture (1 in 12 to 1 in 4). (3) Full-cream dried milk with 1 drachm of cane sugar to 2 oz. of mixture (1 in 32 to 1 in 16). (4) Peptonized or lactified cow's milk with 1 drachm of cane sugar to 2 oz. of mixture (1 in 4 to 1 in 2).

Half-cream dried milk, diluted to reduce the protein to a suitable level, contains too little fat for the healthy premature baby, while humanized dried milk contains too high a percentage of fat. Undiluted whey should not be given, owing to the high percentage of mineral salts (0.65%) and the danger of salt retention and oedema.

Method of feeding.—Breast-feeding: Infants weighing 5 lb. or over may be breast-fed after the first twelve hours. Those weighing $4\frac{1}{2}$ to 5 lb. are usually able to be put to the breast on the fourth or fifth day, and should be fed with expressed milk until then. They should start with one or two breast-feeds daily, and increase gradually. Infants under $4\frac{1}{2}$ lb. may be put to the breast as soon as they can be handled without regurgitating or changing colour.

Hand-feeding: If the infant cannot suck strongly enough to be breast-fed, a bottle is given. If it can swallow, but not suck, it is fed by pipette or spoon; and if it can neither suck nor swallow, it is fed by an œsophageal catheter, passed through the mouth. Nasal feeding should be avoided as the nasal passages are narrow and easily injured and infected. As catheter feeds are not without danger they should only be given by trained staff and they should never be given just to save time and trouble.

In all methods of feeding the head is raised to minimize the risks of regurgitation and otitis media; and the infant is placed on its right side, to reduce pressure on the heart and facilitate emptying of the stomach. Handling is avoided after a feed.

Size and frequency of feeds.—The frequency depends on the amount which can be taken before the child tires. Smaller babies will only take small feeds and must therefore be fed two-hourly, while larger and stronger infants, who take more, may be fed three-hourly. Catheter feeds are usually given at four-hourly intervals, as a relatively large quantity can be given.

Initial feed.—In the case of the smaller infants, inco-ordination of the swallowing reflex persists for some hours after birth and it is wise to delay feeding for at least twelve hours.

Fluid and calorie requirements.—Sufficient food must be given to avoid underfeeding with its dangers of lethargy, fever, cyanosis, loss of weight and dehydration. On the other hand, overfeeding must be avoided with its dangers of gastric distension, cyanosis, and vomiting and diarrhoea, leading to loss of weight and dehydration. In actual practice the dangers of overfeeding are greater than those of underfeeding, and in the City of Birmingham Premature Baby Ward stress is laid on survival and not on rapid gain in weight. Although the majority do better than this, there is no anxiety unless the initial loss of weight continues after the end of the first week, or is greater than $1\frac{1}{2}$ oz. per pound of birth-weight, or the birth-weight is not regained by the end of the third week. It has been found that the best survival rates, the least cyanosis, abdominal distension and gastro-enteritis, and the most consistent gain in weight (slow but sure) are obtained with the following daily quantities of fluid (feed).

By the third to fourth day	— 1 oz. per lb. birth-weight daily
" " seventh "	— 2 oz. " " " " "
" " tenth "	— 2½ oz. " " " " "
" " fourteenth "	— 3 oz. " " " " "
After the fourteenth "	— 3 to 3½ oz. per lb. birth-weight daily

As regards calories, the premature infant requires approximately 40 to 50 calories per pound daily by the end of the second week of life, and after this 50 to 60 calories. These values should only be reached gradually. In practice, if the daily amount of the feed is increased, as suggested in the table, the calories will increase automatically. It is wise to give the lowest caloric value on which an infant will gain satisfactorily, and the calories should not be increased so long as the infant is doing well.

Vitamins.—Vitamins A and D: Vitamin D is of particular importance in the premature baby because of the poor store present at birth and the relatively greater growth after birth. Oil is badly tolerated and the vitamin must be given as a concentrate. A small dose of vitamins A and D is commenced at the end of the first week, and this is increased each day until a daily dose of 3,000 i.u. of vitamin D (plus the associated vitamin A) is being given at the age of 4 weeks.

Vitamin B is essential for growth. The requirements of the premature baby are not yet known, but in Birmingham infants are being given 0.2 mg. B₁, 0.2 mg. B₂, and 3 mg. nicotinic acid daily, from the third day of life.

Vitamin C is required to complete the metabolism of protein (Levine *et al.*, 1939). A dose of 5 mg. of a synthetic preparation (e.g. Celin or Redoxon) may be given on the third day, and the dose increased by 5 mg. per day, until 50 mg. is being given daily. From the age of 4 weeks orange juice may be substituted gradually.

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The administration of œstrin, as advocated by Aschheim (1927) has not proved of value.

Room temperature.—Infants over $4\frac{1}{2}$ lb. often feed better in a cool room (60 to 65° F.).

Body temperature.—When the rectal temperature is below 96° F. the infant feeds badly. A stable temperature between 96° and 98° F. is, however, perfectly satisfactory, and attempts to raise it above this level often prove detrimental as suggested by Blackfan and Yaglou in 1933.

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Dr. J. N. O'Reilly [Abridged]: On analysing the feeding charts of a number of premature babies reared under conditions as nearly standard as was consistent with the progress of each individual, the following six features appeared with such regularity that I have adopted them as guides.

The early needs are very small, but they increase rapidly. This strikes me as a sounder conception than that usually put forward, namely, that the baby requires a high calorie intake, but that this cannot be dealt with during the first ten days.

The requirements at the end of the first three days are approximately 8 drs. of fluid per lb. per day.

The babies start gaining on a feed containing 40 cal. per lb., and 14 drs. of fluid per lb. per day.

Babies weighing over 4½ lb. arrive at this intake by the fifth to sixth day; those under 4½ lb. by the seventh to eighth day.

The feed must be increased gradually to 60 cal. and 22 drs., before the majority will show consistent gains. Individual variations of as much as ± 20% are common.

An average gain of ½ oz. per day is satisfactory, though many do better than this.

I wish to stress that these figures are guides only. None the less, they are sufficiently well established to be used in the construction of a feeding schedule for individual cases.

Feeding schedule.—My general plan is as follows: During the first twenty-four hours, nothing is given by mouth. I find that this has almost eliminated vomiting as a difficulty of the early stages. Cyanotic attacks are also fewer in number. On the second day, glucose saline (1/5 strength saline with 4% glucose), is given in quantity ½ to 2 drachms two-hourly, for six feeds. This is followed by alternate feeds of glucose saline and expressed breast milk ½ to 2 drachms two-hourly, for six feeds. On the third day, E.B.M. ½ to 2 drachms is given at each feed throughout the day. The quantity chosen is that which is thought to be within the capacity of the infant—erring, if at all, on the side of caution—and this is not increased during the transition period.

By this time the baby's vigour will have been assessed, and the rate of increase can be planned accordingly. It is helpful to know that the average baby can arrive at the landmark of 40 cal. per lb. in the time given—five to six days for those of 4½ lb. and over, seven to eight days for those under 4½ lb. No attempt is made to force any baby to conform rigidly to schedule.

If the baby cannot approach the desired rate of intake, gavage is considered. As this involves little effort on the part of the child, the quantities are made to correspond to schedule, with the modification that the feeds are given three-hourly instead of two-hourly. For simplicity, the increments are measured to the nearest ½ drachm.

When the intake reaches the neighbourhood of 40 cal. per lb., the weight begins to rise satisfactorily. Experience shows, however, that this rise will not be maintained. When it starts to falter, I increase the feeds, provided the baby can manage larger volumes. When the intake is about 60 cal. per lb. This increase need not be hurried so long as the weight is maintained. In the later stages, further increases may be necessary to satisfy the baby's hunger. Quite a number of infants, on reaching 5 lb. or over, have demanded as much as 80 to 90 cal. per lb.

Fluid requirements.—Experiments were made to find out if the fluid intake was adequate. Extra fluid was given after the milk feeds in a series of cases. In general, there was no effect either on the weight or on the condition of the patient. The fluid content of the undiluted milk appeared to be sufficient.

There are some exceptions to this general rule. If the intake is smaller than normal, dehydration may occur, and special precautions should be taken with some groups of cases. Small babies, and children born of toxic mothers are particularly liable to dehydration. Additional fluid causes an immediate gain in weight, corresponding to the increased turgor of the tissues, but its continued administration has no effect after the dehydration has been overcome. For babies of under 3½ lb. body-weight, I now regularly

Hand-feeding: If the infant cannot suck strongly enough to be breast-fed, a bottle is given. If it can swallow, but not suck, it is fed by pipette or spoon; and if it can neither suck nor swallow, it is fed by an œsophageal catheter, passed through the mouth. Nasal feeding should be avoided as the nasal passages are narrow and easily injured and infected. As catheter feeds are not without danger they should only be given by trained staff and they should never be given just to save time and trouble.

In all methods of feeding the head is raised to minimize the risks of regurgitation and otitis media; and the infant is placed on its right side, to reduce pressure on the heart and facilitate emptying of the stomach. Handling is avoided after a feed.

Size and frequency of feeds.—The frequency depends on the amount which can be taken before the child tires. Smaller babies will only take small feeds and must therefore be fed two-hourly, while larger and stronger infants, who take more, may be fed three-hourly. Catheter feeds are usually given at four-hourly intervals, as a relatively large quantity can be given.

Initial feed.—In the case of the smaller infants, inco-ordination of the swallowing reflex persists for some hours after birth and it is wise to delay feeding for at least twelve hours.

Fluid and calorie requirements.—Sufficient food must be given to avoid underfeeding with its dangers of lethargy, fever, cyanosis, loss of weight and dehydration. On the other hand, overfeeding must be avoided with its dangers of gastric distension, cyanosis, and vomiting and diarrhoea, leading to loss of weight and dehydration. In actual practice the dangers of overfeeding are greater than those of underfeeding, and in the City of Birmingham Premature Baby Ward stress is laid on survival and not on rapid gain in weight. Although the majority do better than this, there is no anxiety unless the initial loss of weight continues after the end of the first week, or is greater than $1\frac{1}{2}$ oz. per pound of birth-weight, or the birth-weight is not regained by the end of the third week. It has been found that the best survival rates, the least cyanosis, abdominal distension and gastro-enteritis, and the most consistent gain in weight (slow but sure) are obtained with the following daily quantities of fluid (feed).

By the third to fourth day	— 1 oz. per lb. birth-weight daily
" " seventh	— 2 oz. " " " " "
" " tenth	— 2½ oz. " " " " "
" " fourteenth	— 3 oz. " " " " "
After the fourteenth	— 3 to 3½ oz. per lb. birth-weight daily

As regards calories, the premature infant requires approximately 40 to 50 calories per pound daily by the end of the second week of life, and after this 50 to 60 calories. These values should only be reached gradually. In practice, if the daily amount of the feed is increased, as suggested in the table, the calories will increase automatically. It is wise to give the lowest caloric value on which an infant will gain satisfactorily, and the calories should not be increased so long as the infant is doing well.

Vitamins.—Vitamins A and D: Vitamin D is of particular importance in the premature baby because of the poor store present at birth and the relatively greater growth after birth. Oil is badly tolerated and the vitamin must be given as a concentrate. A small dose of vitamins A and D is commenced at the end of the first week, and this is increased each day until a daily dose of 3,000 i.u. of vitamin D (plus the associated vitamin A) is being given at the age of 4 weeks.

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Section of Epidemiology and State Medicine

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[October 27, 1944]

Medical Aspects of Coal-Mining

By S. W. FISHER, B.A., M.D., Barrister-at-law,

H.M. Chief Mines Medical Officer, Ministry of Fuel and Power

IN order to illustrate the conditions which may influence the incidence of the various diseases met with among underground workers in coal-mines Dr. Fisher showed a short film of the men and boys at their work, a coal-cutting machine in action, moving conveyors, a deputy or examiner testing for methane (CH_4 , "Firedamp") and stone-dusting before shotfiring (in order to render the coal dust non-explosive) and various other processes. Dr. Fisher then read his paper, as follows:

Mining hazards fall into two groups: accidents and industrial diseases.

GENERAL

Mines differ greatly; no two are quite alike; they vary in size, some employing less than 10, others 3,000, and in a few cases even more. The depths range from a few yards to well over 1,000 and the distances inbye to the working places may be from two to three or more miles, sometimes going under the sea. In a few mines the wet-bulb temperatures may reach and exceed 85°F. , but this is exceptional.

In 1943, 1,782 coal-mines were working and produced 195 million tons of coal. The average number of persons employed was 701,544, of whom 16,312 were boys under 16. Only 127 females are now employed compared with 2,320 in 1939. Approximately five times as many persons work underground as on the surface.

Women and girls, when employed, mostly work on the screen sorting "rubbish" from the coal as it passes along the screening belts. Their employment underground has been prohibited in this country since 1842, but it was not until over ninety years afterwards that it was secured universally by an International Convention adopted at Geneva in 1935.

ACCIDENTS

The frequency of the occurrence of accidents, their severity and the importance of early treatment at the mine, are matters of great concern. The fact that some time must elapse between the happening of an accident underground and the patient's being seen by a doctor makes a sound first-aid organization necessary, and on the whole first-aid work at mines reaches a high standard

prescribe subcutaneous saline (1/5 strength), 5 to 20 c.c., four to six hourly, given by syringe. This is continued until, together with the fluid taken by mouth, the total intake is about 16 drachms per lb. As the oral intake increases, the subcutaneous injections decrease in number and volume, so that the total remains at the same level. The injections are started on the first day of life, twelve hours after birth. For other babies, additional fluid is given either by œsophageal tube or subcutaneously, according to need, if sucking is too exhausting.

Dehydration may also occur due to overheating. This is apt to happen to small babies in wards where the room temperature is not thermostatically controlled. Extra fluid may cause quite a marked rise in a hitherto unsatisfactory weight chart.

Food.—The next point to decide is what the food shall be. I work principally with breast milk. It is particularly valuable with the smaller and feebler babies. I give it undiluted and I have never seen digestive troubles in consequence.

For the well-established infant, ½-cream Cow and Gate is very satisfactory, and indigestion seldom results. Indeed, digestive upsets have been rare in my whole series, and have usually been attributable to some cause other than the quality of the food.

I have used evaporated milk with success, but have not had occasion for gaining wide experience with it in premature infants. There is, further, the current difficulty of supply.

This brings me to speak of the use of concentrated and fortified feeds. In view of the fluid requirements, I do not find any place for such devices as concentrated milk, either breast or cow's, in the feeding of the normal premature baby. Occasionally, one finds a baby whose weight gain is unsatisfactory, but it has temporarily reached the limit of its capacity to deal with larger volume. In such a case, the addition of soluble protein up to 4%, is a useful way of increasing the calorie value without increasing the bulk of the feeds. I have used soluble protein in a number of cases, and I have been satisfied with the results. The protein is well tolerated, and has never upset the digestion.

The frequency of feedings.—My own practice is to feed all babies two-hourly, until they are thoroughly well established, when a change is made to three-hourly feedings—eight in twenty-four hours. When the infants are being prepared for discharge, the number is reduced to six, and they are discharged on a normal three-hourly schedule.

As many as eighteen feeds in twenty-four hours are recommended by some authorities. I have tried this, but found it impossible wearing both for baby and nurse, and without corresponding advantages. In the other direction, some workers give eight three-hourly feeds from the start. My difficulty is to get the weakly baby to suck long and vigorously enough to ingest the larger feed without fatigue. When the baby cannot suck satisfactorily at all and gavage is employed, eight feeds are all that are necessary. The limiting factor appears to be the baby's energy and not the capacity of its stomach.

The method of feeding.—Most babies of over 5 lb., unless there has been toxæmia, can manage breast-feeding either immediately or after a few days. Of those between 4½ and 5 lb., some can breast-feed without difficulty, while others are better hand-fed. Those below 4½ lb., should be hand-fed until they are well established.

The smallest babies—between 2 lb and 3 lb.—are fed with a pipette until they can suck and swallow easily, when a Belcroy feeder may be tried. From 3½ lb., the babies may have to be pipette-fed for a time, but the majority can take from a Belcroy feeder quite soon. Between 3½ lb. and 4½ lb., the babies can manage a Belcroy feeder from the start, and the larger ones soon do better on a bottle.

The weakly babies who tire rapidly before they have taken a full feed are something of a problem. I think that most pædiatricians are somewhat prejudiced against gavage except as a last resort. I certainly share the prejudice, but in skilful and careful hands there appears to be little against it. Sufficient food can be introduced rapidly and with little fatigue to the patient. I still feel, however, that gavage should never be permitted merely as a convenience to the nurse.

Miscellaneous.—A few miscellaneous points remain to be mentioned. I add iron at 3 weeks if the digestion is stable. This is necessary to prevent the anæmia which is constantly present from getting worse. It may have a disappointingly small effect in actually raising the hæmoglobin percentage. Vitamin C is also added at this time—particularly if there is any addition of protein to the feeds. Vitamin D is included as soon as it is judged that the digestion will stand it. I have not found thyroid very helpful. I have used it in a number of cases where the baby has been sluggish, but I have not found that there has been any appreciable improvement in the clinical condition or in the weight chart. Vitamin K is given in the labour theatre to all premature babies.

(Charts were shown illustrating the progress of babies of different weights, fed according to the scheme outlined.)

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An interesting experiment is being made at present at a number of collieries of allowing specially selected and instructed first-aid men to administer a quarter of a grain of morphia to severely injured or burned men. The control both of the first-aid men and the drug is very strict and only one injection may be given—the drug must be provided in ampoule-syringe form. All reports on this experiment have been highly encouraging.

The number of accidents in the year 1943 was 713 fatal and 173,716 involving an absence from work for three or more days. Every effort is being made to ensure that severe accidents receive good surgical treatment and accident rehabilitation centres have been opened in the various coal-fields with the object of obtaining the maximum degree of restoration of function.

INDUSTRIAL DISEASES

The mining industrial diseases scheduled under the Workmen's Compensation Act are: miners' nystagmus, beat hand, beat knee and beat elbow, inflammation of the synovial lining of the wrist-joint and tendon sheaths, dermatitis, spirochaetal jaundice and ankylostomiasis (there have been no cases of ankylostomiasis reported in British mines since 1917).

The disease pneumokoniosis is not scheduled under the Act in the ordinary way, but power is given to the Secretary of State to make special schemes of compensation for workmen employed in mines who contract the disease as a result of their employment.

The incidence of these diseases in 1943 is shown in the following table:

CASES IN WHICH CERTIFICATES OF DISABLEMENT WERE GIVEN IN 1943.*

Pneumo- koniosis (new cases)†	Nystagmus	Beat hand	Beat knee	Beat elbow	Inflammation of wrist	Derma- titis	Spiro- chaetal jaundice
1,322	2,006	606	5,300	1,044	438	1,207	9

* Provisional figures.

† This does not include death certificates for men who have previously been certified as disabled.

Pneumokoniosis.—This is probably the most interesting mining disease from a medical point of view. The occurrence of silicosis has been recognized among coal-miners for many years, but the early cases were men who had done a fair amount of mechanical drilling in hard siliceous rock like that of the Pennant series of South Wales or the Greys of Somerset. The condition found both radiologically and pathologically resembled to a certain extent silicosis as found in the Rand gold-mines. That is to say the presence of nodular fibrosis was distinguished, which advanced to consolidation and in some cases cavity formation. The main symptom was marked dyspnoea, and emphysema with heart failure was frequently thought to be the cause of death. This incidentally differed somewhat from the South African silicosis, where the end-result was mostly pulmonary tuberculosis.

As time went on, however, a new type of case was met with in the South Wales coal-mines. The cases reported seemed of a more chronic type, and the X-ray appearance of the lung fields showed reticulation, with or without nodulation. The reticulation was rather like the X-ray appearance of "arborization" found among the Rand miners at an early stage.

Perhaps the most striking thing about the South Wales cases was the working history. The men who complained of breathlessness, it was found on inquiry, had not worked with boring machines in rock, but were simply colliers working at the coal-face, getting coal and shovelling it on to conveyor belts.

This information led to the exhaustive investigations by the Medical Research Council in 1936, the result of which showed that a large proportion of colliers, chiefly, but not only, in the anthracite area, gave the X-ray picture of reticulation and that this condition can be disabling. The recognition of this fact led to a widening of the compensation term from silicosis to pneumokoniosis, and applied to all underground workers.

So far there is no definite evidence that reticulation must inevitably lead to nodulation but it would seem that it may do so, particularly if the man goes on breathing harmful dust, and the more dust he breathes the more likely it is that reticulation will develop.

Much more work has yet to be done on this type of pneumokoniosis; the incidence is heavy, the economic burden great and the anxiety among the South Wales miners acute.

There are plans for following up ex-miners who have left the industry on account of pneumokoniosis and who are now working in other trades. Already some interesting facts about these men have been collected. A long-term investigation is contemplated whereby the physical condition of working miners will be correlated to the environmental conditions of their places of work. In addition to this all new entrants to the industry in South Wales are to be X-rayed.

Much attention is being directed to prevention and the results of the present methods are promising.

It is hoped that research will indicate some form of treatment and general improvement of the patients; for instance, the application of the results of Canadian and American workers on the effects of the inhalation of aluminium dusts as a prophylactic measure may be tried out on selected cases.

The Coal Mines Act, 1911, Section 78, enforces the use of water sprays or jets or other efficient safeguards when drilling in ganister, hard sandstone or highly siliceous rock, the dust from which is liable to give rise to fibroid phthisis. The amending of this Section is contemplated in the light of further knowledge and as more effective measures are perfected. At present water infusion, wet cutting, foam, mist projectors, face masks and exhaust dust traps and collectors are made use of at suitable places (slides shown).

Miners' nystagmus.—This complex disease shows itself principally by a rotatory oscillation of the eyeballs. The oscillation affects both eyes and according to Dr. Wellwood Ferguson does not resemble nystagmus due to other causes, excepting perhaps congenital nystagmus. Miners' nystagmus does not lead to blindness as many miners fear. A comparison of the oscillations of miners' nystagmus and other types is rather well shown in a film (shown later) kindly lent by Dr. Wellwood Ferguson. Many disturbing phenomena accompany the oscillations such as photophobia, the "dancing" of objects looked at, insomnia, and in some cases extreme depression. Oscillations in a mild form cause little or no disability but the headaches, insomnia and depression do. There is much work to be done both as regards the physiology and pathology of the condition but up to the present it is agreed by most authorities that the fundamental cause of miners' nystagmus is insufficient illumination at the place of work. This theory is borne out by the almost complete absence of nystagmus in mines where the illumination permits central vision to function. Posture, as seen in the film on coal-mining and various slides, may also be possible factors when lighting is poor. As much light is absorbed by dark surfaces, especially the coal-face itself, Regulations require, in all mines under the Coal Mines Act in which the total number of persons employed exceeds ten, that certain parts of the mine shall be effectively whitewashed (the effect of this is seen in the slides shown). Broadly speaking, remedial treatment of a patient consists in taking him out of the mine for a period and providing him with work in good light as soon as possible, and by allowing him ultimately to return underground in a place where there is adequate illumination.

It will be interesting to observe what effect the remodelling of the Workmen's Compensation Act will have on the course of the disease.

Beat hand, beat knee, beat elbow and inflammation of the synovial lining of the wrist-joint and tendon sheaths.—The total numbers of cases in 1943 were: Beat hand 696, knee 5,300, elbow 1,044, wrist-joint 438.

The diseases popularly known as "beats" are compensable under the Workmen's Compensation Act, 1925, and are scheduled under the following descriptions: subcutaneous cellulitis of the hand (beat hand); subcutaneous cellulitis or acute bursitis arising at or about the knee (beat knee); over the elbow (beat elbow); inflammation of the synovial lining of the wrist-joint and tendon sheaths.

In the case of the knee and elbow the trouble is caused by constant friction against a hard surface. Infection can gain entrance through a minute scratch or through the sodden skin if conditions are wet, and an inflammation of the part follows. In the case of the hand, continual jarring by the handle of the pick, especially if it is rough, damages the tissue and again renders it liable to infection and inflammation. The wrist and tendon conditions are also caused by repeated small shocks and excessive tendon movements. The effect of subcutaneous cellulitis and synovitis is of comparatively short

duration, namely from three to four weeks in the case of beat knee and beat elbow and rather longer in the case of beat hand.

Prevention: Beat knee may be avoided by the use of kneeling pads of various descriptions, special care being taken to prevent minute coal particles from being rubbed into the skin. Similar care of the elbow will also have a beneficial result. Regulations do not enforce the use of knee or elbow pads, but recommendations following an inquiry by the Medical Research Council (Report 1924) were brought to the notice of the industry (M.D. Circular No. 14). Attention to the handle of the pick, i.e. seeing that it is smooth, will also help to avoid beat hand, and in all cases examination and care of minute abrasions when the working shift is over are of great importance. Their early treatment can easily be carried out at mines where pithead baths are installed or at the surface ambulance rooms. Good general health is important, and medical treatment should be sought at the earliest sign of inflammation.

Infective Jaundice (*Spirochaeta jaundice*; *spirochaetosis icterohaemorrhagica*; *Weil's disease*).—This disease is caused by the micro-organism called *Leptospira* or *Spirochaeta icterohaemorrhagiae*. It has been notifiable in Scotland since 1924, but not in England and Wales, and has been recognized for some years in many countries. Compensation is now payable provided that the diagnosis is confirmed by bacteriological or serological examination.

As far as coal-mines in Great Britain are concerned cases have been reported in Scotland, Northumberland and Durham and a few in South Wales. The disease as found among miners does not differ in any way from that found among other persons.

When making investigations into the disease among coal-miners I have observed that wherever cases have arisen, the presence of rats is nearly always established and the working places in the mines are wet. It has been shown that, at certain mines where men who have contracted the disease have worked, rats caught in the mines have harboured the *Leptospira*, and in one case the organism was isolated from the jelly-like slime that clung to the timber. Moreover, the workings in the mines whence cases have been reported are usually shallow and nearly always communicate with the surface by a drift or level. This fact may be of interest inasmuch as not only may rats enter the mine, but they can easily leave it and go, for example, to a river, farm or dwelling-house, returning to the mine at will. Surface water (which may be contaminated) penetrates into shallow mines with comparative ease; for instance, a definite increase of water is sometimes noticeable at the melting of a heavy fall of snow. On the other hand, rats are present in many mines both shallow and wet at which, as far as is known, no cases of infective jaundice have occurred, although it is recorded that a proportion (up to 40%) of all rats harbour the organism.

The diagnosis of the disease can be made with some certainty by means of bacteriological or serological tests. Certain manifestations are usually associated with it, namely, fever, with severe pain and muscular tenderness, congestion of the conjunctiva, jaundice, and hemorrhages under the skin from the mucous membrane. The disease may be fatal, or it may be so mild as to be missed owing to the absence of jaundice; in fact, blood specimens from a number of men working in the same part of a mine were found to be positive although some of the men had shown no clinical signs of the disease; the incubation period averages about ten days.

The organism may enter the body through abrasions in the skin, through the alimentary tract from contaminated food, or through the mucous membrane of the nose. One miner with whom I spoke attributed his attack to water which he had splashed up from the road in the mine into his face and mouth.

As it is the general opinion that the disease is transmitted from rats to men, the first and most important preventive measure in mines is to rid them of rats. This matter is receiving attention with the collaboration of the Infestation Branch of the Ministry of Food.

Dermatitis.—Dermatitis attributable to working conditions is less frequent than might be expected in an industry which is dusty and in which the workers are brought into contact with so many different objects. The factors which have been put forward as causes of dermatitis (a) and the preventive measures (b) which have been suggested are as follows:

(A)	(B)
(a) Tinea pedis among users of pit-head baths.	Thorough drying of feet after bathing. Dusting between toes with a powder, e.g. mixture of zinc oxide, boric acid and starch; swilling out of baths by an antiseptic solution, excluding workers affected from use of baths.
(b) Ringworm contracted from pit ponies.	Medical treatment of both pit ponies and persons affected.
(c) Strong acid or alkali solutions among lamp-room attendants.	Possibly a "barrier" substance; careful washing in running water.
(d) Grease and oils.	Possibly a "barrier" substance; careful washing in running water.
(e) High wet-bulb temperatures (over 75° F.).	Improvement of ventilation if sluggish.
(f) Handling of wet cement (e.g. when sinking shafts).	Thorough washing and drying of hands and arms at end of each shift.
(g) Water rich in chlorides; on floor or from roof.	Measures determined by circumstances.

As many cases become disabled through secondary infection, men with any type of skin lesion or abrasion are encouraged to make early use of the surface ambulance room at mines. A large proportion of cases must be due to non-industrial causes for it cannot be expected that miners are immune from skin diseases such as scabies, eczema, impetigo, and psoriasis.

HIGH TEMPERATURE IN MINES

The effect on workers of natural high temperatures in mines is largely one of economic importance, but it must also be considered from the point of view of health. Much work has been done on high temperatures in mines, but up to the present no enforceable standards of wet- and dry-bulb temperatures or of ventilation have been recommended.

The problem of fixing legal standards is difficult because several factors are interdependent. It is agreed that the dry-bulb temperature is of less importance than the wet-bulb temperature, because it is the continuous cooling of the skin by evaporation of sweat which is of significance.

It must be recognized that there is a fundamental difference between a man and a thermometer. For a given set of conditions a thermometer always gives the same result; but man has the power to adapt himself to environment—a phenomenon known as acclimatization. In hot mines this manifests itself by control of body temperature through increase in the amount of sweat given off, so that an acclimatized miner does not show the rise of body temperature which might occur in an unacclimatized man; he sweats sufficiently to allow his skin to remain comparatively cool by evaporation, provided that an adequate air current is available.

It may be observed that where men sweat in an atmosphere of high wet-bulb temperature, and where sluggish ventilation minimizes the evaporation of sweat from their bodies, there is a tendency for men to develop skin rashes and boils. This is noticeable from 75° F. wet-bulb upwards. To render conditions in a hot mine as healthy and comfortable as possible, suitable limits of wet- and dry-bulb temperatures and rate of air current passing over the workers should still be sought. Heavy sweating and drinking large amounts of water may cause muscular fatigue and even severe cramp. Most men who are inconvenienced in this way can improve their condition by drinking less water and by adding a little salt (half a teaspoonful to a pint of water) in order to restore the normal chloride concentration. This is being done at some mines.

MEDICAL SERVICE FOR MINERS

The medical facilities available to miners are (a) their panel doctors, (b) hospital services, and (c) rehabilitation centres.

Owing to the close communities of mining areas the panel doctor is familiar with the work of miners and the diseases and accidents to which they are liable. In this respect

miners are somewhat more fortunate than a large proportion of factory workers. The same applies to a lesser extent to the hospitals to which miners are sent. Generations of miners have been attended to by generations of doctors, most of whom have been underground at some time or other to attend to accidents.

A few mines employ a full-time doctor who keeps a general eye on all health matters.

Covering all this is the Mines' Medical Service of the Ministry of Fuel and Power consisting of nine doctors in the coal-producing regions and two at headquarters. These doctors have had experience among miners and by virtue of their office are able to visit all types of mines and, therefore, gain the broad knowledge of underground conditions which is so essential to their work.

Their function is mainly advisory and consultative and directed towards the investigation of the causes of industrial disease and methods for their prevention. They link up with the miner's doctor, the hospital and the rehabilitation centre. They are in no way interested in questions of compensation.

Dr. G. F. Keatinge said that he had been somewhat disappointed that no reference had been made to the incidence of psychosomatic disease in the coal-mining industry. It was undoubtedly high and the industrial unrest only too common amongst miners was probably largely a psychological phenomenon.

It was unreasonable to think that the mining community as a whole was fundamentally less well balanced from a psychological point of view than other sections of the population. It was therefore a fair assumption that the frequent occurrence of psychosomatic disease in the miner was the result of the conditions under which he had to work.

The problem of reducing the incidence of psychosomatic disease and indeed disease in general in colliery work could be faced in two ways. The first method was to select suitable new entrants to the industry by physical and psychological examination. The second and better approach was to improve the conditions under which the men worked.

Dr. Fisher had mentioned various measures to improve conditions but technical difficulties surrounded the introduction of some of them: flood lighting of the coal-face, for example, was not easy.

Improvements in working conditions could only be in the nature of a long-term policy but there was one important way in which they could be improved at once and that was to reduce the working week from six shifts to five. The opinion was widely held in the coal-mining industry itself that the high rate of absenteeism amongst miners was the result of too long hours.

A previous speaker had asked whether any attempt had been made to immunize miners against tetanus as was done in the Services. Dr. Keatinge had considered this, but thought that the very small number of miners who became infected hardly warranted the time and trouble involved even if the miner would agree; Dr. Keatinge shared Dr. Fisher's admiration of the miner but he was by nature rather suspicious of new ideas.

In those collieries for which he was responsible and in which a nursing service had been introduced, A.T.S. was given as soon as a casualty reached the first-aid room, but all the collieries were within twenty minutes' journey of a general hospital where it was given as a routine if it had not been given earlier.

Clinical Section

President—J. D. ROLLESTON, M.D.

[November 10, 1944]

Three Cases shown by IVOR M. ROBERTSON, F.R.C.S.Ed.

(1) Acute Osteomyelitis Right Ilium.

E. L. C., male, aged 10.

History.—13.3.44: Sudden onset of pain in right hip followed by tonsillitis. Admitted to hospital on 16.3.44, complaining of pain in left ankle and right ankle. T. 103°, pulse 100. Diagnosed as acute rheumatic fever. Given salicylates and later sulphathiazole 6.5 g.

24.3.44: Transferred to another hospital. T. 103°, pulse 100.

Diagnosis.—Septicæmia secondary to osteomyelitis ilium. ? infection right hip-joint. W.B.C. 20,400. Blood culture: *Staph. aureus*.

28.3.44: Bronchopneumonia developed. Sulphathiazole 33 g. given over five days.

31.3.44: Transferred to Hill End Hospital. Critically ill, delirious. T. 104°, pulse 136, respirations 36. Right hip held flexed and abducted and intense muscle spasm. All movements resisted and extremely painful. Right ilium: Considerable thickening over crest of ilium which was painful on pressure particularly posteriorly. Abdomen: Large mass of deep iliac glands palpable and tender. Blood culture: *Staph. aureus*.

Penicillin—continuous intramuscular drip commenced immediately (500,000 units given in eleven days).

18.4.44: Double hip spica applied for ten weeks. The temperature gradually fell during the next six weeks and his general condition improved correspondingly. The osteitis of right ilium, as shown by X-ray, spread to involve the whole of the ala but the infection never localized, no sinuses appeared and no surgery was required. The deep iliac glands and all reflex spasm disappeared.

10.11.44: Completely recovered. Hip movements normal. X-ray appearance shows considerable sclerosis of right ilium.

(2) Acute Osteomyelitis Right Tibia.

B. W., male, aged 5.

History.—Ten days before admission to hospital knocked right leg against a wall. Leg became painful and pain increased in severity, becoming localized below right knee. Six days later patient developed fever and vomited.

10.2.44: Transferred to Hill End Hospital. Ill child. T. 101°, pulse 130. Right leg: Knee held in flexion and whole region of knee-joint and upper third of tibia red and swollen. Area of most acute tenderness over upper end of tibia. Glands palpable and tender in groin. 14 g. sulphathiazole in four days prior to admission.

Operation (10.2.44).—Upper end of tibia explored. Large subperiosteal abscess evacuated. Bone drilled—wound lightly packed and plaster applied with windows. Peni-

DEC.—CLIN. 1

cillin: continuous intramuscular drip commenced immediately. 440,000 units given over period of eleven days. Culture of pus—*Staph. aureus*—coagulase positive. Blood culture sterile.

On tenth day after initial operation wound was sterile. Secondary suture was performed and through a small rubber tube inserted in upper end of wound penicillin was instilled daily. A total amount of 36,000 units was used over period of eleven days. At the end of that time the tube was removed and the wound was soundly healed in twenty-six days from time of initial operation. X-ray changes were minimal.

10.11.44: Wound has remained healed. X-ray appearances show some sclerosis of upper third of tibia but no sequestrum formation.

(3) Acute Osteomyelitis Left Radius.

R. G., female, aged 3.

History.—Six days before admission fell down on left arm. X-ray negative. Six days later pain was much more severe and further X-ray showed area of osteitis at lower end of radius. Transferred to Hill End Hospital.

Clinical features.—12.5.44: On admission child looked ill in spite of normal temperature and pulse. Left forearm: Brawny fluctuant swelling over whole length of radius, but most acutely tender over lower end.

Operation.—Large subperiosteal abscess evacuated. Periosteum found stripped over whole length of diaphysis which appeared to be completely surrounded by a bag of pus. Bone appeared white and dead. Wound lightly packed and closed plaster applied. Penicillin: Continuous intramuscular drip commenced immediately. 500,000 units given over period of eleven days. Culture of pus—profuse growth of *Staph. aureus*—coagulase positive. Blood culture sterile.

At the end of six days wound was still infected but in spite of this secondary suture was performed on the seventh day. A small rubber tube was left in upper end of wound and penicillin instilled locally. A total amount of 6,000 units was used over a period of ten days. The tube was gradually withdrawn and the wound was healed in eighteen days.

X-ray showed considerable osteitis over whole length of shaft of radius with periosteal reaction.

10.11.44: Wound has remained healed. X-ray appearances show regeneration of radius with sclerosis, but no sequestrum formation.

Two Cases shown by P. H. BEALES, F.R.C.S.Ed.

(1) Osteomyelitis of Tibia.

P. C. D., aged 16. Factory worker.

History.—Six days before admission he got a wood splinter in left arm. This became septic and was treated by nurse at factory as a boil. Three days before admission he had severe pain in left knee-joint and could only walk with difficulty. A day before admission: Very hot and shivering, restless and mentally confused.

18.9.44: Admitted complaining of pain in left leg.

Temperature 102.6°, pulse 104, respirations 22. Very ill and confused boy. Skin flushed and dry. Tongue filthy, gums dry and cracking. Scab on left arm. L. axillary glands palpable.

Left knee-joint: Held in slight flexion; movements full but slightly painful. No evidence of free fluid in the joint. Glands enlarged and tender in left groin. Blood culture: Pure growth *Staph. aureus*. Traction to left knee-joint. Sulphathiazole 2 g., followed by 1 g. four-hourly. Total sulphathiazole 16 g. over two days.

19.9.44: Scab raised from left arm, underneath was a small cavity containing pus which gave a profuse growth of *Staph. aureus*.

20.9.44: Still very ill. Area of slight reddening and oedema over medial aspect upper shaft of left tibia. Penicillin: 100,000 units daily in 500 c.c. sterile water, given by continuous intramuscular drip in upper thigh—leg changed alternate days. No local reaction at injection sites. Total systemic penicillin 500,000 units.

21.9.44: General condition improved, but complaining of considerable pain in left tibia.

Operation.—22.9.44: Drainage of subperiosteal abscess upper end left tibia. Pus found under considerable tension. 2 drill holes down to medulla. Wound packed with gauze and immobilized in plaster of Paris splint. Bacteriology: Many pus cells and Gram-positive cocci in small clumps. Cultures: Aerobic and anaerobic sterile.

23.9.44: Free of pain. Temperature normal.

25.9.44: Penicillin discontinued.

4.10.44: *Secondary suture of drainage wound.* Skin edges freed and sutured over a multihole rubber catheter through which 3 c.c. penicillin solution (strength 1,000 units per c.c.) was run into the wound six-hourly for three days. Total local application penicillin 36,000 units over three days.

23.10.44: X-ray report: Subperiosteal calcification upper third medial side tibia, an oval fairly well-defined area decreased density in cortex medial side upper third tibia and below this another area less well defined. No sequestrum seen.

30.10.44: Discharged from hospital. Wound practically healed.

(2) Acute Osteomyelitis of Tibia and Femur.

D. G. L., aged 12. Schoolboy.

History.—Ten days before admission he banged his right knee cap when jumping a ditch. Two days later he felt ill and feverish and was put to bed; his right leg became very painful two to three days later and he became very ill with profuse sweating.

21.9.44: Admitted complaining of pain in right leg. Temperature 100.6°, pulse 114, respirations 24. Ill-looking boy, flushed and sweating. Tongue furred. Right knee and ankle joints swollen. Right leg œdematous and flushed. Point of exquisite tenderness on medial side of upper quarter shaft of tibia.

X-ray: ? focus of infection lower end shaft of femur. No changes in tibia.

A diagnosis of acute osteomyelitis of tibia and ? lower end of shaft of femur was made and in view of the clinical findings immediate operation was performed.

Operation.—21.9.44: (a) Drainage of lower end right femur $\frac{1}{2}$ in. hole drilled through to medulla. No pus obtained. Culture sterile. (b) Drainage upper half tibia. Large amount of pus was found under the periosteum which it had stripped over a wide area. A hole drilled through to medulla and a quantity of pus escaped under pressure. Incisions packed with gauze. Plaster of Paris splint. Culture sterile (probably faulty technique in taking of swab in view of later bacteriology).

Penicillin: 100,000 units daily in 500 c.c. sterile water, given by continuous intramuscular drip for five days, following operation. Intramuscular drip in upper thigh; leg changed each day. Total systemic penicillin 500,000 units. No local reaction at injection sites.

22.9.44: Free of pain.

23.9.44: General condition satisfactory but still pyrexial.

26.9.44: As the temperature had not subsided packing was removed from tibia and some pus escaped. Wound repacked.

27.9.44: Temperature normal.

4.10.44: *Secondary suture wounds.*—(a) Incision over femur clean; closed by interrupted sutures. (b) Subcutaneous pocket of pus was found extending upwards and medially from the upper end of the tibia. This was drained by a small incision through the skin. Wound sutured over a multihole rubber catheter through which penicillin 3 c.c. (1,000 units per c.c. sterile water) was run in every six hours for three days. Total local application penicillin 36,000 units in three days.

Bacteriology of wounds.—(a) Femur: Few Gram-positive cocci in pairs and clumps. Culture sterile. (b) Pus from subcutaneous pocket upper end tibia. Many pus cells, very many degenerate Gram-positive cocci mainly in pairs. Culture—scanty growth *Staph. pyogenes*. (c) Sequestrum from tibia taken from region of drainage hole in bone. Many pus cells, few degenerate-looking Gram-positive cocci mainly in pairs. Culture: Many colonies *Staph. pyogenes*.

23.10.44: X-ray shows uneven density with subperiosteal calcification upper half of tibia; no sequestrum seen. Also uneven density lower fibula.

30.10.44: Wound over femur healed. Wound of tibia practically healed; ambulant.

Staphylococcal Arthritis of Left Hip Treated by Large Doses of Sulphathiazole.— R. PARKINSON, F.R.C.S.

A. A., a boy, now aged 9 years.

16.7.42: Admitted to hospital with a three days' history of pain in the upper left thigh becoming worse. No known trauma or septic focus.

On admission.—Very ill, toxic child. Temperature 105°, pulse 140, respiratory rate 24. The only physical sign was a tenderness of the upper half of the left thigh, maximal in the region of the hip-joint; he resented any attempt at movement of the hip. There was no visible swelling of the area. The left lower limb was immobilized on a Thomas's splint and he was given sulphathiazole 1 g. four-hourly and remained on this dose for nine days.

Blood culture taken on the day of admission grew *Staph. aureus*, 45 colonies per c.c. The white cell count was 34,300 per c.mm. with 86.5% polymorphs. 17.7.42: Staphylococcal antileucocidin 0.04 K (normal 0.01-0.08). On 17.7.42 and again on 19.7.42 he was given 20,000 units of staphylococcal antitoxin. His general condition improved slowly—locally, he developed a fullness around the left hip-joint and particularly below the inguinal ligament with evidence of a brawny cellulitis, but there was never evidence of fluctuation.

20.7.42: Blood culture showed four colonies of *Staph. aureus* per c.c. 23.7.42: One colony per c.c. Staphylococcal antileucocidin 0.64 K. 30.7.42: Blood culture was sterile. The general condition continued to improve steadily—the local physical signs remained unchanged, and he was next immobilized on a Robert Jones' double abduction frame.

27.7.42: X-ray showed no gross change in the left hip or related femoral neck, apart from slight irregularity at the lower margin of the latter (1st X-ray).

30.7.42: Staphylococcal antileucocidin 3.0 K.

7.8.42: Twenty-six days from the onset of the disease, changes were evident in the left hip-joint (2nd X-ray). Immobilization was continued by means of the abduction frame and after two months in hospital the boy was afebrile, very cheerful and eating well.

9.9.42: A third X-ray showed the femoral head subluxated. On account of this the boy was then immobilized in a hip spica plaster following reduction of the subluxation under anaesthesia. He remained in the plaster in bed for a further three months. Eight months after his illness began he was allowed up with crutches, still in plaster. This was removed two months later and he was allowed home with a patten to the other leg and crutches.

19.7.43: One year after the onset of the disease, he was readmitted with a history of an abscess in the left groin, bursting four days previously. Further immobilization in plaster for two months resulted in the discharge ceasing completely, and the groin wound has remained soundly healed ever since. He was finally discharged with a walking caliper, which he is still wearing.

Serial X-rays show the progressive change in the left hip-joint towards a bony ankylosis with absorption of the femoral head.

Three Cases by E. C. B. BUTLER, F.R.C.S.

(1) Staphylococcal Septicæmia. Osteomyelitis of Pelvis. Recovery.

M. P., female, aged 9.

5.9.42: Admitted with three days' fever, delirium and pain in the left hip.

On examination.—Delirious girl, tender over iliac crest, no obvious primary focus. Blood cultures: 5.9.42: 65 colonies per c.c. of blood. *Staph. aureus* (Dr. Valentine). 7.9.42: 97 colonies. 9.9.42: Sterile.

Treatment.—(1) Two injections of intramuscular antitoxin. (2) Sulphathiazole. 2 g. four-hourly for a total dosage of 96 g. No toxic effects. (3) Pelvis and legs immobilized in a double abduction splint with traction. (4) Fluids plus by mouth.

On the day before her blood became negative she pulled out a loose tooth, culture from the socket grew *Staph. aureus*. This may have been the primary focus.

16.9.42: Drainage of an abscess over the ilium. *Staph. aureus*. X-ray: Obvious disease of ilium.

29.9.42: X-ray showed infection had spread into the hip-joint.

23.12.42: Splint discarded after drainage of two more abscesses. Hip spica applied. After this steady improvement.

Present condition.—Walks well and there is slight movement in the hip-joint. Other movements at pelvis. Slight discharge from posterior sinus.

(2) Staphylococcal Septicæmia. Osteomyelitis of Femur. Penicillin Therapy.

Girl, aged 9.

Ten days: Boil on nose. Four days: Increasing pain in right thigh.

18.10.44: Ill but not delirious. T. 103°, pulse 130. Signs of acute infection upper third right femur. Blood culture: 60 colonies of *Staph. aureus* per c.c. of blood.

Treatment.—Leg and pelvis immobilized. Continuous intramuscular penicillin 85,000 units every twenty-four hours for five days.

23.10.44: Condition good, still a little tenderness over right femur. Course of sulphadiazine given (46 g. in four days). Temperature and pulse normal after 26.10.44.

1.11.44: All signs of infection gone. Splint removed.

X-ray: No evidence of bone infection.

(3) Anaerobic Infection of the Finger. Systemic Penicillin.

Coloured woman, aged 32.

Six days before admission she was bitten on the index finger by a man.

On examination.—5.10.44: She was an ill woman. T. 99°, pulse 110. Left index finger was swollen, oedematous and foul-smelling. The site of the bite was discharging offensive pus. The dorsum of the hand and the thenar space were swollen with oedema. The axillary lymphatic glands were enlarged and painful. Culture of the pus: Aerobic—*Staph. aureus*. Anaerobic—*Streptococci* and fusiform bacilli. Penicillin-sensitive.

Treatment.—Local: The finger was immobilized on a plaster splint. Penicillin cream was applied every other day. General: 160,000 units of Canadian penicillin were given every twenty-four hours for six days. The drug was given by repeated intramuscular injections of 20,000 units every three hours. No local pain was experienced until the last day. At the end of her course she felt well, the finger was of normal size and all the swelling of the hand had gone. The infection had not spread but the terminal phalanx had nearly separated from local necrosis at the site of the bite. Culture: A few anaerobic streptococci remained.

8.11.44: The terminal phalanx has gone leaving a clean granulating wound. The rest of the hand is quite normal.

Comment.—Anaerobic infection of the hand generally follows human or cat bites.

The causative organisms are generally a mixture of anaerobic streptococci and fusiform bacilli. The outlook in the past has been bad. Several deaths have been reported and in other cases multiple operations were often required before the spread of the infection could be arrested.

I have seen two cases before, one was in a lunatic asylum, and he eventually died after amputation of his arm. The other man recovered after extensive incisions had been made into his hand.

This patient recovered without any surgical treatment other than removal of the necrotic terminal phalanx at the site of the original bite.

Mr. A. Dickson Wright: This case is of great importance as these infections are notoriously indolent and destructive. They are also incurred by throat surgeons and dentists when working on lightly anesthetized patients, and similar trouble is encountered with cat and monkey bites. The trouble is probably due to anaerobes and the Vincent's symbiosis, and these, it seems, respond readily to penicillin.

Interauricular Septal Defect. Hæmoptyses. —WILFRED STOKES, M.D.

A. H., female, aged 34.

History.—Frequent coughs followed pneumonia at age of 2 years. Slight cyanosis after exertion in childhood. "Rheumatic fever" at age of 23. Since the age of 26

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Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[November 7, 1944]

Congenital Pseudarthrosis of the Tibia Treated by Twin Grafts

By S. ALAN S. MALKIN, M.B., B.S., F.R.C.S.Ed.

DIFFERENCES of opinion exist as to whether or not congenital pseudarthrosis of the tibia is a clinical entity. In this paper the term is used because it is generally accepted as meaning a condition occurring in early childhood—it will be agreed that its treatment is always a difficult problem.

Probably the best results until recently have been obtained either by using the fibula as a reinforcement of the tibia or by placing a tibial graft posterior to the fracture in such a way as to short-circuit and buttress it.

In 1941 Boyd published a paper on this subject, and reported a series of cases in which he had used dual tibial grafts which, in order to obtain sufficient bone, had been taken from one of the parents of the child and had been fixed by vitallium screws.

In 1942 there were admitted to Harlow Wood Orthopædic Hospital two children with pseudarthrosis of the tibia, both of whom had been previously treated elsewhere. For both we decided to use twin tibial grafts.

For some years, when fusion of the tubercular hip is needed, in certain cases, we have adopted Brittain's (1942) ischiofemoral method. It will be remembered that Brittain devised a special technique for obtaining massive tibial grafts. This consists of exposing the shaft of the bone, stripping the periosteum and removing a segment which includes the anterior crest, the medial surface, and the medial margin of the tibia. (We have in adults not used both the anterior crest and the medial margin.) It may be said that taking such a large piece of bone from a normal tibia may seriously affect it, but this has not been our experience, although it is of course necessary to protect the bone for a period after the operation. We felt that if we used this type of graft we should be able to avoid the necessity for taking a graft from one of the parents.

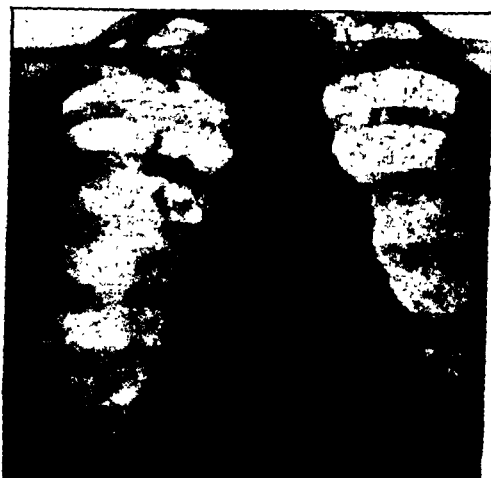
CASE I.—The first patient was a boy aged 6½ who, it was stated, at the age of 3 months had been noticed to have a fractured tibia for which he had had treatment at various hospitals. He was admitted to Harlow Wood when 6½ years old, at which time he had a considerable deformity of his leg, due to a pseudarthrosis.

Although we had decided to treat the condition with twin grafts, prior to this grafting operation, an attempt was made to manipulate the bone into a better position, without much improvement.

On March 15, 1943, the pseudarthrosis was exposed and excised, together with the fibrous tissue round it, and a tibial graft, cut from the other tibia by the method already described, was applied as two lateral onlay grafts held in position by two vitallium screws, one above and one below the fracture. By this means the grafts were firmly fixed. The region between the grafts was packed with cancellous bone. Plaster of Paris was applied to both legs.

cough with sputum throughout the year, with hæmoptyses up to one cupful. The sputum was reported generally to be yellow, up to one cupful in twenty-four hours. Recently dyspnœa has been caused by walking even short distances.

On examination.—Small stature, with faint cyanosis of lips and prominent sternum but no clubbing of fingers. Normal rhythm. Splitting of first sound throughout præcordium, but no murmur or thrill. Pulmonary second sound accentuated. B.P. 140/70. Variable rhonchi throughout the chest. Poor basal air entry. Cardioscopy: Prominent right auricle and pulmonary artery. Slight left auricular curve outlined by barium in the œsophagus in both oblique positions. Marked hilar dance. No hilar congestion.



Interauricular septal defect with severe hæmoptyses. (Postero-anterior position.)

Electrocardiogram: T inverted in III and diphasic in CRI., R.E.A.D., T₂ well up. No bundle branch block. Bronchogram: No bronchiectasis demonstrated in either lung.

Comment.—Cases of interauricular septal defect exhibiting no murmurs are infrequent. It is usually presumed that the defects in such cases are large; yet the degree of right heart stress, as judged from the radiographic and cardiographic findings does not appear to be more than moderate in this instance. The hæmoptyses were more severe than one expected from the degree of pulmonary artery enlargement. Bronchiectasis has been excluded by full bronchography, and the hæmoptyses must be ascribed directly to the morbus cordis.

Dr. Eli Davis raised the question of associated mitral stenosis, but in reply Dr. Stokes was confident that this was not a case of Peacock's (Lutembacher's) syndrome because of the absence of murmurs in normal rhythm.

(The report of this Meeting will be concluded in a later issue.)

Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[November 7, 1944]

Congenital Pseudarthrosis of the Tibia Treated by Twin Grafts

By S. ALAN S. MALKIN, M.B., B.S., F.R.C.S.Ed.

DIFFERENCES of opinion exist as to whether or not congenital pseudarthrosis of the tibia is a clinical entity. In this paper the term is used because it is generally accepted as meaning a condition occurring in early childhood—it will be agreed that its treatment is always a difficult problem.

Probably the best results until recently have been obtained either by using the fibula as a reinforcement of the tibia or by placing a tibial graft posterior to the fracture in such a way as to short-circuit and buttress it.

In 1941 Boyd published a paper on this subject, and reported a series of cases in which he had used dual tibial grafts which, in order to obtain sufficient bone, had been taken from one of the parents of the child and had been fixed by vitallium screws.

In 1942 there were admitted to Harlow Wood Orthopædic Hospital two children with pseudarthrosis of the tibia, both of whom had been previously treated elsewhere. For both we decided to use twin tibial grafts.

For some years, when fusion of the tubercular hip is needed, in certain cases, we have adopted Brittain's (1942) ischiofemoral method. It will be remembered that Brittain devised a special technique for obtaining massive tibial grafts. This consists of exposing the shaft of the bone, stripping the periosteum and removing a segment which includes the anterior crest, the medial surface, and the medial margin of the tibia. (We have in adults not used both the anterior crest and the medial margin.) It may be said that taking such a large piece of bone from a normal tibia may seriously affect it, but this has not been our experience, although it is of course necessary to protect the bone for a period after the operation. We felt that if we used this type of graft we should be able to avoid the necessity for taking a graft from one of the parents.

CASE I.—The first patient was a boy aged $6\frac{1}{2}$ who, it was stated, at the age of 3 months had been noticed to have a fractured tibia for which he had had treatment at various hospitals. He was admitted to Harlow Wood when $6\frac{1}{2}$ years old, at which time he had a considerable deformity of his leg, due to a pseudarthrosis.

Although we had decided to treat the condition with twin grafts, prior to this grafting operation, an attempt was made to manipulate the bone into a better position, without much improvement.

On March 15, 1943, the pseudarthrosis was exposed and excised, together with the fibrous tissue round it, and a tibial graft, cut from the other tibia by the method already described, was applied as two lateral onlay grafts held in position by two vitallium screws, one above and one below the fracture. By this means the grafts were firmly fixed. The region between the grafts was packed with cancellous bone. Plaster of Paris was applied to both legs.

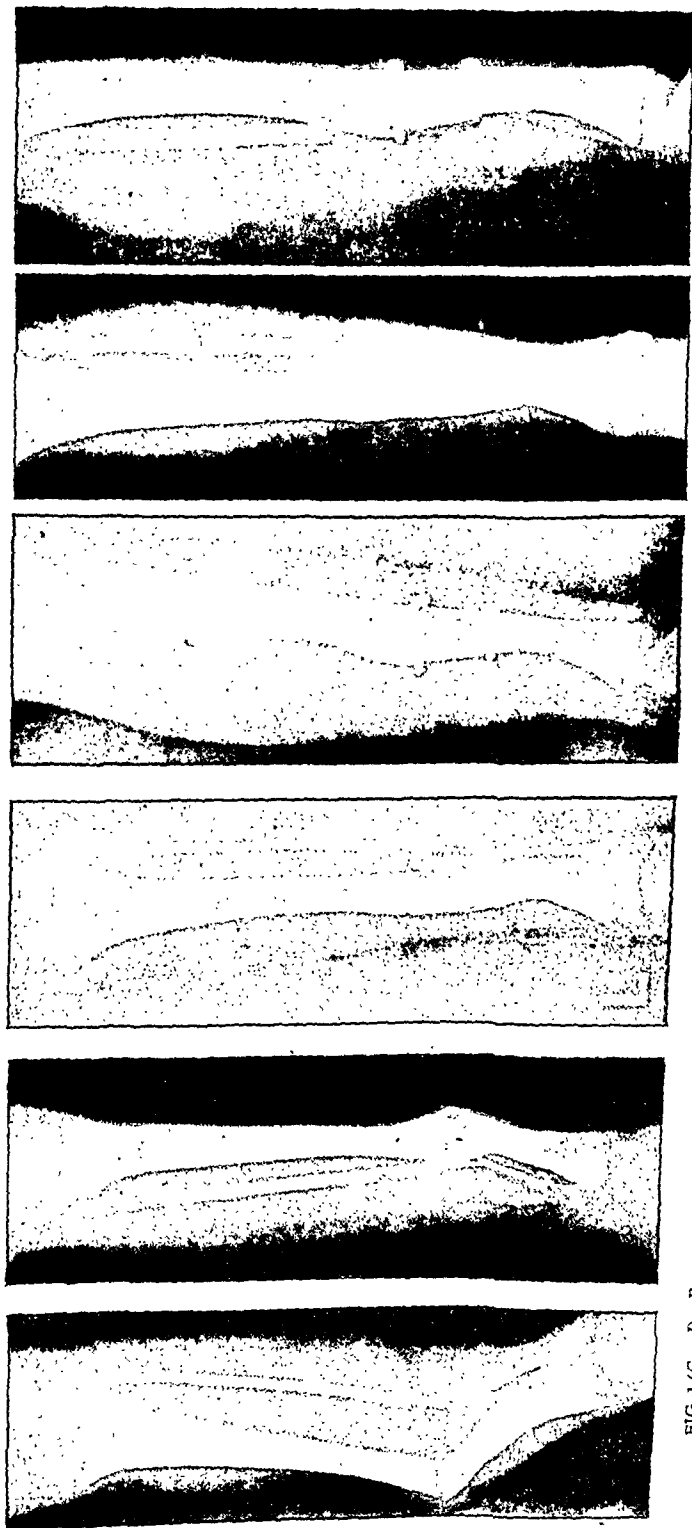


FIG. 1 (Case D).—Preoperative X-ray.

FIG. 2 (Case D).—X-ray taken eleven months after the grafting operation.

FIG. 3 (Case D).—X-ray taken eighteen months after operation.

MALKIN: Congenital Pseudarthrosis of the Tibia treated by Twin Grafts.



FIG. 5 (Case II).—X-ray taken seventeen months after grafting operation.



FIG. 4 (Case II).—Preoperative X-ray.



MALKIN: Congenital Pseudarthrosis of the Tibia treated by Twin Grafts.

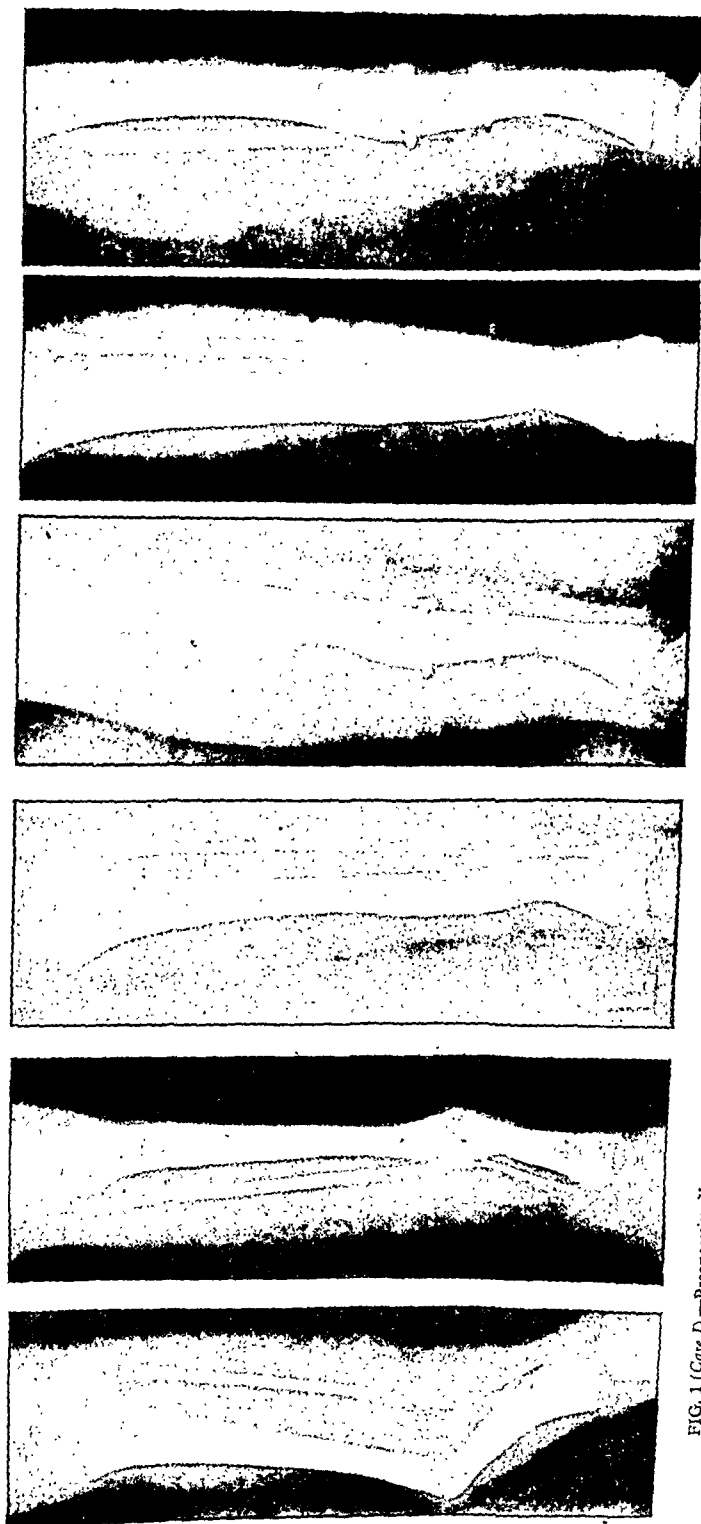


FIG. 1 (Case 1).—Preoperative X-ray.

FIG. 2 (Case 1).—X-ray taken eleven months after the grafting operation.

FIG. 3 (Case 1).—X-ray taken eighteen months after operation.

MALKIN: Congenital Pseudarthrosis of the Tibia treated by Twin Grafts.

of one bone or part of one bone from the proximal row of the carpus does not affect this relaxation of the tissues and is therefore unlikely to relieve the pain. The necessary gap can only be obtained by removing the whole of the proximal row. In the case of an ununited fracture of the scaphoid, the removal of one or both fragments will only relieve pain due to shearing stresses across the fracture line. Often, however, this is not the only cause of pain, hence the uncertainty of the result.

In the second place, the removal of either the scaphoid, or the semilunar, completely upsets the complicated mechanism of the wrist; it is bound to result in weakness and is likely to set up new stresses which may cause pain. If the normal mechanism of the wrist is to be ruined in any case, it is surely necessary to see that it is replaced by some other and simpler mechanism. The simplest machine which works is better than a complex one which is out of order.

Excision of the whole of the proximal row of the carpus offers a possible solution to both these problems, for it not only provides a good joint gap, but also results in the substitution of a simple ball-and-socket joint between the os capitatum and the radius for the normal complicated link-joint mechanism.

It may be argued that this procedure is too radical. It is, however, an accepted principle of surgery that, while early treatment should be conservative, late treatment must be radical if it is to be effective. Moreover, it is in effect a reconstructive operation for it provides a new and simplified wrist-joint, whereas partial excisions are purely destructive procedures.

The operation itself is a simple though tedious one, since great care must be taken not to damage the radius or the other carpal bones. The after-treatment is all important. I favour ten days complete rest in plaster, followed by very gentle, coaxed, active movements, at first only one or two movements in each direction twice a day. The wrist is immobilized on a plaster slab between treatments. Active exercises of the fingers are encouraged from the beginning. After three weeks, preliminary hot soaks may be given with light massage, the movements being gradually increased in range and frequency. During the four to six week period an inflammatory reaction may occur as so often happens in all arthroplasties at this period. All treatment must then be stopped for three to four days. The final result cannot be expected in less than four months.

I have been able to observe the results over periods of up to five years and they have on the whole been sufficiently good to encourage me to use the method more rather than less often, and also to give this interim report in the hope that the method may receive a more extended trial.

A good result gives a painless wrist with a grip almost equal to the normal and with 65% to 70% of the normal range of movement. It must be remembered that the normal wrist consists of a double or link-joint, whereas the new joint is a simple hinge, and is therefore incapable of developing the same range of movement. 70% of the normal is the maximum possible and is its full range. Unless this is appreciated attempts may be made to increase the range still further, which can only result in damage being done to the joint.

The average result is a wrist with 50% to 70% of the normal range of movement, slight weakness of grip as compared with the opposite side, and occasionally some degree of pain on forced radial deviation of the wrist. I think this must be due to impaction of the carpus on the styloid process of the radius. It is rarely sufficient, however, to interfere with function. I have had one or two complete failures. In each case there was some damage to the articular surface of the radius, either as a result of comminuted fracture or traumatic arthritis.

It is not yet possible to say how long the new joint will last. At the worst, however, even if arthrodesis should ultimately prove necessary, it will have been greatly facilitated by the removal of the proximal row of the carpus.

Its chief indications are for cases of weak and painful wrists following ununited fractures of the scaphoid and avascular necrosis of the semilunar, when the preservation of some mobility of the wrist is necessary for the individual to be able to return to his former employment, and it appears unlikely that the removal of one bone or one fragment will be sufficient to relieve pain. It is contra-indicated in those cases where the articular surface of the radius is damaged or arthritic, and is probably inadvisable if the patient does heavy manual labour.

In four months the bone was found to be united, and a walking plaster was applied—the boy was later supplied with a caliper. He is now walking without any support and the fracture is firmly consolidated with about 1½ in. shortening. Fig. 1 shows the preoperative condition, fig. 2 the condition eleven months after the grafting operation, and fig. 3 eighteen months after the grafting operation.

CASE II.—The second case was a girl aged 7. When 2 years old she was said to have fractured her left leg. She was treated at home and later admitted to a hospital where two bone-grafting operations were carried out, unfortunately without success. She was subsequently fitted with a gaiter and caliper and continued so until she was 7 years old. She was then sent to the Harlow Wood Orthopædic Hospital, and on admission was found to have 3 in. shortening of the leg, and pseudarthrosis of the tibia.

We felt that a leg so short, even if the bone could be made to unite, would be a great handicap. At a preliminary operation, therefore, we divided the pseudarthrosis and by gradual traction with turnbuckles, by the method of Alcorn (1938) we lengthened the limb and so reduced the shortening to ½ in.

The grafting operation was performed on May 27, 1943, by my colleague Gilbert Parker. In this case, a graft taken from the opposite tibia was divided diagonally so forming two grafts. The broader ends of these grafts were fixed to the proximal fragment of the tibia, the pointed ends to the distal fragment. The bone was so soft that screws were not used, stainless steel wire fixing the upper ends of the graft, the lower ends being implanted into the distal fragment. Between the grafts cancellous bone was packed. The limb was fixed in plaster and four months later the tibia was found to be firmly united.

Protection was continued for some months after this. The fracture has remained united and has become gradually more consolidated. There is now 1½ in. shortening—some of the length originally gained was subsequently lost. Fig. 4 shows the preoperative condition, fig. 5, seventeen months after the grafting operation.

Comment.—Circulation of the lower third of the tibia is notoriously poor and it may be that this and the strangulation of single grafts by scar tissue, and the difficulty of adequate fixation account for some of the lack of success in the past in treating congenital pseudarthrosis of the tibia. The twin grafts firmly applied form a protective scaffolding for the cancellous bone packed between them and a buttress against the strangulation by scar tissue. This may allow circulation to be developed and maintained, and new bone to be formed with subsequent healing of the fracture.

Time will show whether this combination of Brittain's method of cutting from the other tibia a massive tibial graft with Boyd's plan of using twin grafts between which cancellous bone is packed is, in fact, the solution of this difficult problem. At least it may be said that it is a method which can be used in dealing with considerable bone loss in certain of the long bones.

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Excision of the Proximal Row of the Carpus

By T. T. STAMM, F.R.C.S.

WHEN a wrist has become weak and painful as a result of such conditions as ununited fracture of the scaphoid or Kienböck's disease, the restoration of useful function presents a very difficult problem, but it is one of considerable importance from the economic point of view. In many cases arthrodesis affords the best solution since it is the only method by means of which a strong and painless wrist can be guaranteed. In many trades, however, such as that of a mechanic, a fixed wrist is a considerable disability, and some power would willingly be sacrificed for mobility, provided that a painless grip could be retained. The so-called conservative procedures, however, such as the removal of part or the whole of one of the bones, give uncertain and, in many instances, disappointing results.

In the first place, the pain must be due either to stretching or to compression of sensitive tissues. The object of treatment must therefore be to restore a free range of movement, throughout which no structures are submitted to excessive stretching or impaction. Thus the essential step in any arthroplasty is to provide a gap whose closure will relax the surrounding structures and so relieve the tissues from stress. The removal

excised uncompromisingly—the whole track, if possible, should be excised right down to the depths of the wound with the aid of retractors: in the perforating wound each side of the thigh should be dealt with separately so that at the end of the operation a complete track exists through the thigh. The object should be to allow free and unhindered drainage without any danger of "pocketing."

(Coloured lantern slides were shown illustrating "Tobruk plasters" and thoraco-humeral plaster box.)

Six patients with fractured femoral shaft required amputation, 2 on account of the severity of the injury involving the knee-joint, 2 on account of gas gangrene infection and 2 on account of vascular gangrene.

Twelve patients with established gas gangrene infection were encountered; 4 massive infection of the lower limb, 8 with localized infection of which 7 had a muscle group involved while 1 patient had the *Clostridium* infection confined to the subcutaneous tissue only. 5 of the cases were associated with fracture; 7 with soft tissue wounds involving thigh or buttock muscles. Cultures from many wounds revealed the presence of *Clostridium welchii* without any clinical evidence of established infection.

These patients had been wounded several days previously and they had lain about in open country with deep soft tissue wounds with a certain amount of hæmorrhage. On arrival their general condition was recorded as poor; much rapid resuscitation was required to fit them for operation; all made satisfactory recoveries, except one who arrived moribund and died before any treatment could be instituted.

The appearance of the flesh wound did not always reveal the true nature of the underlying condition in the limb, e.g. a soldier arrived with an apparently healthy excised posterior thigh wound but in a poor general condition; in view of this latter state exploration of the wound was determined—the whole of the hamstring muscles were found gangrenous and required excision from buttock to behind the knee. Incidentally this soldier had received a considerable amount of penicillin but the circumstances were such that his primary operation had been inadequate.

Number of patients :		
Treated
Suffering from compound fractures
(No. of compound fractures 176)	...	245
Suffering from multiple soft tissue wounds	...	138
Suffering from chest wounds	...	50%
Suffering from abdominal injuries	...	40
Suffering from spinal column injuries	...	37
Suffering from maxillo-facial injuries	...	10
Miscellaneous conditions	...	9
	...	7
	...	4
	...	12%

Fifteen patients with vascular injuries to the limbs were encountered; 5 in the upper and 10 in the lower limb; 11 of these cases developed gangrene of the distal portion of the limb—this is rather surprising considering that these patients were healthy young subjects whose collateral circulation should be adequate when the main vessel of a limb is occluded. Concomitant damage to soft tissue causing thrombosis in the surrounding vessels and extending to the collateral circulation no doubt contributed to the production of gangrene. Associated injury to accompanying peripheral nerves has the same effect by sympathetic stimulation causing spasm in the collateral circulation, e.g. A soldier was admitted with a cold useless right upper limb following on a mortar bomb wound in the right axilla. Exploration revealed a piece of metal lodged in the third part of the axillary artery and pressing on the brachial plexus; removal of the metal revealed the necessity of ligaturing the vessel. Within a few hours the limb was warm, without pain and had recovered its function. The irritation to the brachial plexus had been removed and with it the sympathetic stimulation to the collateral circulation. Again, of 3 cases of ligature of the brachial artery in the middle of the arm in almost precisely the same place and with approximately the same amount of soft tissue wound, 2 patients with peripheral nerve injury developed gangrene of the hand, while the remaining patient who apparently had no nerve injury suffered no gangrene.

With distal gangrene of a limb and with a more proximal compound fracture it was considered unwise to wait a lengthy period of time for a line of demarcation to develop for the deep recesses of the wound soon became infected owing to diminished vitality; pus

Certain Observations on Normandy Casualties [Abridged]

By DAVID TREVOR, M.S., F.R.C.S.

THE majority of the work encountered at a Port Hospital on the South Coast in connexion with casualties from Normandy in the few weeks immediately succeeding D-Day consisted of dealing with compound fractures (56%), with multiple soft tissue wounds (16%) and with chest wounds (16%); thus 88% of the 245 patients dealt with personally fell into these three groups.

Resuscitation was an important part of the early treatment of these wounded soldiers; in most cases resuscitation had begun on the beaches in Normandy or in the L.S.T.s while crossing the Channel; many of the wounded had received several pints of blood before admission to the Port Hospital and required yet further transfusion before being fit for operative treatment. The large amount of blood that appeared necessary and was accommodated comfortably by the men was astonishing, e.g. a marine with multiple injuries including an abdominal injury required 22 pints over a period of sixteen days before being fit to travel further inland.

The cases requiring a good deal of resuscitation were those suffering from traumatic amputation of one or both limbs, compound fractures, gas gangrene infections and obviously where much blood had been lost such as in multiple soft tissue wounds. The blood was transfused at a moderate rate; few dangers were encountered, but care was taken not to transfuse many pints of blood to patients suffering from blast injury effects, or to patients suffering from chest wounds for fear of precipitating pulmonary oedema which actually happened in one case.

Rest was an important factor in recovery, for some of the wounded had been engaged in heavy fighting for several days without any sleep, and subsequent to being wounded, had experienced a rather uncomfortable journey across the Channel lying on a hard stretcher in some instances for two or three days. A few hours' sleep on a comparatively soft bed improved their general condition remarkably.

Chemotherapy was carried out on the wounded unless contra-indicated; as a prophylactic 25 to 30 g. of sulphathiazole were given over a period of five days; but with heavy wound infection the dosage was increased to a much greater quantity over a shorter period of time. In cases of multiple soft tissue wounds it was important to realize that 10 to 15 g. of sulphathiazole could easily be insufflated into one wound, e.g. extensive thigh or buttock wound; so that during the whole operation the patient would probably receive 30 to 40 g.; obviously this was to be avoided.

Where there was the least likelihood of *Clostridium* infection anti-gas gangrene serum in large doses, 100,000 to 150,000 units in three doses, were given in the blood drip. In addition penicillin as the sodium salt in solution was given intramuscularly at three-hourly intervals in doses of 15,000 units over a period of four or five days.

Amongst the compound fractures dealt with were 40 patients with 41 compound fractures of the shaft of the femur. Irrespective of the site of fracture they could be classified into two groups. The majority had a perforating wound, a small entry and a large rugged exit wound; the thigh had a certain amount of swelling but there had been some subcutaneous drainage and decompression of the thigh by reason of laceration and destruction of the tight fascial band around the thigh by the exit wound, with the result that the tenderness and associated pain were not nearly so much as in the other type where an entry wound existed alone. In this latter group the penetrating wound had produced a small skin lesion, a small hole in the fascia which prevented any subcutaneous drainage; furthermore it was generally found blocked by a piece of swollen muscle thereby sealing the track; consequently the interior of the thigh where there was a good deal of muscle destruction and hæmorrhage became an incubator—for all infected foreign material such as dirt, clothing, &c., carried in by the missile was retained. In this type of case the thigh, unless adequately and early decompressed, rapidly becomes the site of an anaerobic infection. Unless this is appreciated the small skin wound may be adequately dealt with, but the small fascial wound considered of no great importance and adequate decompression of the thigh neglected.

These compound fractured femurs should be regarded as an extensive muscle injury rather than a bone injury; the skin and fascial wounds should be incised for an adequate length in the long axis of the limb, the fascia being again divided transversely at each end of the wound; the damaged muscle and all retained foreign material should be

of the vertebræ in this situation. The patient lies on his back and these plaster beds are very comfortable (figs. 2 and 3).

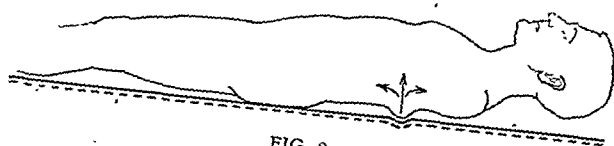


FIG. 2.



FIG. 3.

Head and pelvic traction.—When there is a cervico-dorsal or high dorsal disease or when there is paraplegia the employment of head and pelvic traction in addition to a plaster bed of the above type is advisable. This traction can be applied by means of webbing straps. In the appliance for the head it is very important that the strap going below the occiput meets the strap going round the forehead at an angle above each ear. The lateral straps pull vertically on the junction of the occipital and forehead straps, so that the obtuse angle becomes less obtuse and the head is gripped (see fig. 4).

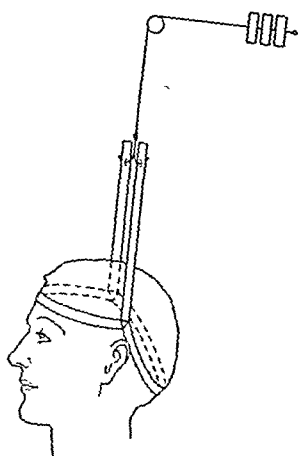


FIG. 4.

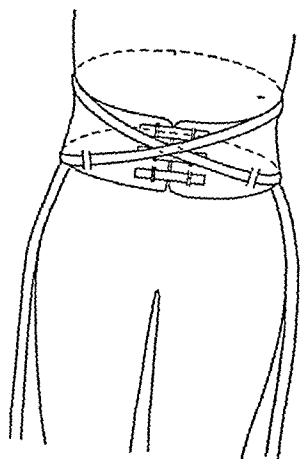


FIG. 5.

The pelvic belt should be fitted round the waist so that it covers the iliac crests. In addition to the ordinary buckles, an oblique strap is added on each side. Each of these pull the belt in above each iliac crest, so that traction is made against the iliac crest and no amount of force can dislodge it (see fig. 5). I am indebted to Sir Henry Gauvain who taught me the use of this appliance.

Adhesive traction to limb.—Dr. W. T. Gordon Pugh taught that adhesive strapping should not be applied to a limb in lateral strips, as oblique wrinkling of the skin is caused and early sore formation. Application of adhesive material in the form of a sleeve gives better results. The method to be described I first saw Mr. E. S. Evans use at Carshalton. Two pieces of stockinet are fitted to the limb reaching from the upper part of the thigh to half-way down the calf. They are sewn together at their lower or distal ends. To the circumference of this junction of the lower ends of the stockinet are attached

would then track upwards in the limb in the deep tissue space causing toxæmia although superficially the wound seemed unchanged.

Lastly, 3 cases of compression fracture of the lumbar spine with associated abdominal symptoms and signs were admitted; they complained of abdominal pain, while examination of the abdomen revealed board-like rigidity and tenderness simulating an acute abdomen; however, their general condition was good and there was no free fluid in abdomen, no diminished liver dullness or tenderness *per rectum*. During the next twenty-four hours a certain amount of abdominal distension occurred which responded to continuous gastric suction, &c., and from here on the abdominal condition gradually subsided and disappeared.

Looking back through records of cases seen in the past I remember a woman admitted to hospital in a moribund condition suffering from abdominal pain and tenderness following on an injury to her back; before anything in the nature of resuscitation could be performed she died. Post-mortem revealed a fractured spine with extensive retroperitoneal hæmorrhage. A similar case was recently under the care of a colleague at the Port Hospital where there was an extensive retroperitoneal hæmorrhage but no intra-abdominal lesion to account for the abdominal symptoms. Therefore I venture to suggest that the cause of these complicating abdominal signs and symptoms in cases of fractured lumbar spine is probably due to an extensive retroperitoneal hæmorrhage which is found in the first few hours after sustaining a compression fracture of one of the lumbar vertebrae causing irritation of the posterior parietal peritoneum.

I wish to thank the Director-General of the E.M.S. for permission to publish this paper.

Some Methods of Non-Skeletal Traction

By M. C. WILKINSON, M.B., B.S.

CERTAIN methods of non-skeletal traction may prove very effective. They have been used chiefly in the treatment of skeletal tuberculosis but may be applied successfully to other conditions.

Distraction of vertebral bodies by plaster bed.—During the active progressive phase of tuberculosis of the spine it is necessary to separate the diseased vertebral bodies and to hold them immobilized. It is possible to achieve this with precision by means of a plaster bed. The patient is laid on his face. Pieces of felt are laid on the patient's back above and below the kyphos, so that a flat surface is formed. A complete layer of felt is then laid over all from the base of the neck to the bend of the knees. Plaster is applied and moulded in as well as possible (fig. 1).

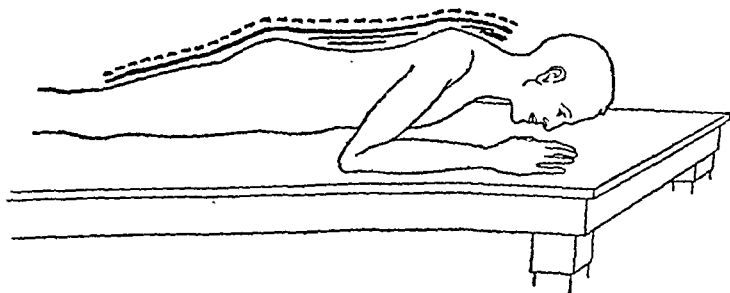


FIG. 1.

When the plaster has set and been mounted on a wooden frame, the additional pieces of felt are removed: the plaster is smoothed, and a small gutter made for the apex of the kyphos, if it is sharp. A felt lining is left in. The patient's back becomes moulded to the shape of the bed as he lies in it. Forces acting on the kyphos effect distraction

Section of Medicine

President—GEOFFREY EVANS, M.D.

[October 24, 1944]

DISCUSSION ON GASTRITIS

Dr. T. Izod Bennett: The subject of gastritis is one very difficult to approach because the scientific physician feels that nothing is known of its ætiology, its morbid anatomy is obscure, symptoms are often entirely absent, the prognosis is doubtful and, in fact, the one thing about which we can speak with certitude is the treatment—there is none. Very much the same thing could be said about diseases such as measles and “catarrhal” jaundice; indeed as regards the latter disease it is obvious that if bilirubin had happened to be a colourless substance the diagnosis of this disease could never have been made clinically.

It remains a strange fact that textbooks and books on gastro-enterology have printed articles on gastritis for many decades of which it can be said with truth that there is no scientific basis whatever; even during the present war articles have appeared on dyspepsia as a source of invalidity in the Services in which it has been written that gastritis is a common cause of disability; in the course of a considerable experience during the same period the speaker has not once succeeded in definitely establishing a diagnosis of gastritis in any member of the Services suffering from dyspepsia. At the present day the diagnosis of gastritis must rest principally upon gastroscopy although, for reasons to be given later, even gastroscopic diagnosis must be accepted with reserve.

If we review the more important work on gastritis by past observers we must never forget that Samuel Fenwick in 1877 discovered that persons suffering from pernicious anæmia had a strange gastric atrophy; he made this discovery by immediate post-mortem examination of the gastric wall of persons dying from various diseases associated with cachexia. The late Professor Knud Faber pursued similar researches for many years; he regarded gastritis as a fairly common condition affecting the stomach wall in a manner analogous to that fibrotic change which we call cirrhosis of the liver. The writer has never been able to find a recognizable symptomatology for the condition described by Knud Faber.

The advent of fractional gastric analysis led to recognition of the relative frequency of the condition named achylia gastrica. In 1921 the speaker called attention to the occasional occurrence of this condition in subjects whose health was apparently perfect, and the work of Bennett and Ryle on normal medical students suggests that complete achylia gastrica is present in 3 or 4% of normal healthy young adults. It is regrettable that the gastroscopists have not yet investigated such cases but it is certain that they occur and that at any rate for many years their health may remain unimpaired. Why indeed should a person suffering from severe gastritis have any symptoms? Whatever may be views concerning total gastrectomy we must all admit that it is not infrequently performed with success and that there is a considerable proportion of patients who, after

two strips of finely woven brown holland. Each strip is shaped to half the circumference of the stockinet, one on each side. The other ends of the holland strips are shaped to pass through slots in the stirrup or foot-piece to which the weight can be attached. Each of the two layers of stockinet is then rolled back from its upper end to its lower, in the form of a cuff.

Adhesive paste is then applied to the limb. The first layer of paste is painted on the skin. The lower layer of stockinet is unrolled over the paste up the limb. A second layer of paste is applied over this layer of stockinet. Then the second cuff of stockinet is unrolled up the limb. Thus finally over the skin the layers are, first paste, then stockinet, then paste again, then stockinet again (*see fig. 12, Nursing Mirror, 1943, Suppl. Oct. 30, vol. 78*). The formula for the paste used is given in Bühler's book and is similar to Unna's except that there is a higher percentage of gelatine. The formula is: Zinc oxide 1 lb.; Gelatine 2 lb.; Glycerine 4 lb.; Water 3 lb.

The paste comes from the dispensary in the form of a cake and has to be melted down. This method has been used in certain hospitals for skin traction on amputation stumps.

Traction to reduce flexion deformity of the knee.—This method is especially useful in that it prevents backward displacement of the head of the tibia, or if that is present already, it reduces it. A Thomas' splint is fitted to the limb with a bend at the knee slightly less than the angle of the deformity. Body-weight traction is applied, care being taken to keep a tight band behind the tibial head. In this position the patient's weight exerts considerable pressure through the band across the splint behind the tibial head. The angle of the splint is decreased each day (*see fig. 15, Nursing Mirror, 1943, Suppl. Oct. 30, vol. 78*).

Section of Medicine

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[October 24, 1944]

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It remains a strange fact that textbooks and books on gastro-enterology have printed articles on gastritis for many decades of which it can be said with truth that there is no scientific basis whatever; even during the present war articles have appeared on dyspepsia as a source of invalidity in the Services in which it has been written that gastritis is a common cause of disability; in the course of a considerable experience during the same period the speaker has not once succeeded in definitely establishing a diagnosis of gastritis in any member of the Services suffering from dyspepsia. At the present day the diagnosis of gastritis must rest principally upon gastroscopy although, for reasons to be given later, even gastroscopic diagnosis must be accepted with reserve.

If we review the more important work on gastritis by past observers we must never forget that Samuel Fenwick in 1877 discovered that persons suffering from pernicious anæmia had a strange gastric atrophy; he made this discovery by immediate post-mortem examination of the gastric wall of persons dying from various diseases associated with cachexia. The late Professor Knud Faber pursued similar researches for many years; he regarded gastritis as a fairly common condition affecting the stomach wall in a manner analogous to that fibrotic change which we call cirrhosis of the liver. The writer has never been able to find a recognizable symptomatology for the condition described by Knud Faber.

The advent of fractional gastric analysis led to recognition of the relative frequency of the condition named achylia gastrica. In 1921 the speaker called attention to the occasional occurrence of this condition in subjects whose health was apparently perfect, and the work of Bennett and Ryle on normal medical students suggests that complete achylia gastrica is present in 3 or 4% of normal healthy young adults. It is regrettable that the gastroscopists have not yet investigated such cases but it is certain that they occur and that at any rate for many years their health may remain unimpaired. Why indeed should a person suffering from severe gastritis have any symptoms? Whatever may be our views concerning total gastrectomy we must all admit that it is not infrequently performed with success and that there is a considerable proportion of patients who, after

this operation, are symptomless. It is therefore abundantly clear that the mere destruction of the gastric mucosa may not produce obvious symptoms.

Great care must be taken in drawing conclusions from the observations of the gastroscopists. The late Sir Arthur Hurst, speaking at the last meeting of the Gastro-Enterological Club, directed attention to the remarkable studies recently published by Wolf and Wolff in a book entitled "Human Gastric Function". This work contains most important observations on a man who for forty-seven years had had a permanent gastrostomy following a traumatic œsophageal stricture. He was a big strong man in perfect health and it was not only possible to observe the gastric mucosa protruding from the wound, but it was very simple to pass endoscopic instruments into the stomach. The observers carried out an enormous number of experiments amongst which some are of immense importance when discussing the problem of gastritis; for example, it was noted that when under the stimulus of food, alcohol, or certain strong emotions such as resentment, the secretion and movements of the stomach were immensely increased and the mucosa became hyperæmic, turgid, and engorged; its folds were thick, red and succulent and minute hæmorrhages would appear not only when the mucosa was touched by a glass rod, but even spontaneously; in fact all the characteristics of so-called hypertrophic gastritis were present. On the other hand, the introduction of air under a pressure not exceeding that which is sometimes reached during gastroscopy was sufficient to flatten out the stomach lining entirely and to produce an appearance of so-called atrophic gastritis.

These observations must warn us against the extreme danger of drawing conclusions from a single gastroscopic examination of any subject and it is scarcely necessary to say that, if gastroscopy is to be performed at least twice, the difficulties of this method of examination are more than doubled.

The radiological diagnosis of gastritis will be discussed by Dr. Cordiner.

Schindler and his collaborators wrote in 1937 "chronic gastritis is a very frequent and often a very severe disease". This ridiculous assertion epitomizes the literature which has so long misled us in our search for knowledge of this obscure subject.

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Dr. F. Avery Jones: The gastroscopic diagnosis of gastritis is beset with difficulties. The changes in appearance simulating gastritis may be summarized as follows:

Appearances of gastric mucosa	Name	Possible cause
Normal		
Thicker and less even than usual	Hypertrophic mucosa (fig. 6)	? normal variation
Thinner and smoother than normal	{ Simple atrophy (fig. 1) Chronic atrophic gastritis (fig. 2)	? trophic change Post-inflammatory atrophy
Redder than normal, more swollen and with excess of mucus	{ Emotional change Gastritis (figs. 3, 4, 5)	Anger, sustained resentment Chemical or bacterial irritation

It is important to realize that the regular "pebble beach" appearance is not inflammatory but a mere rugosity of the mucosa, as shown by Magnus and Rodgers (1938) and I have confirmed this in eight resection specimens. An irregular lumpy coarse "pebble beach" appearance can certainly be produced by inflammation and may be seen near a gastric ulcer (fig. 5). Again, diffuse atrophy is not necessarily inflammatory but can result from a trophic change, possibly endocrine or nutritional in origin. This has been recognized by Hiltenbrand (1930) and Magnus (1937). A further pitfall in diagnosis is the mucosal change which can occur with emotional upset, particularly sustained resentment, when the mucosa becomes turgid, hyperæmic, with excess of mucus (Wolf and Wolff, 1943).

Although this factor is sometimes difficult to exclude, there are cases in which, gastritis can be diagnosed with a high degree of probability, but as a diffuse process causing symptoms it does not seem to be common.

(Figs. 1—6 appear on the coloured plate facing.)



FIG. 1.—Smooth mucosa with uniform atrophy. Blood-vessels very easily seen. Probably simple atrophy from trophic changes.



FIG. 2.—Localized atrophy of anterior wall. Patchy appearance. Blood-vessels visible. Probably post-inflammatory atrophy. A gastric ulcer is also present.



FIG. 3.—Atrophic mucosa with intense hyperæmia and excessive mucus, suggestive of acute gastritis.



FIG. 4.—Intensive hyperæmia with excess of mucus and bubbles suggestive of acute gastritis.



FIG. 5.—An irregular lumpy coarse "pebble beach" appearance. A true "hypertrophic gastritis" proved histologically.



FIG. 6.—Regular "pebble beach" appearance. A constitutional change and not inflammatory in origin.

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Much difficulty has arisen from the classification of gastritis.

Schindler's scheme has become the basis of an immense literature.

SCHINDLER'S CLASSIFICATION OF GASTRITIS.

Acute gastritis	{	Simple exogenous
		Corrosive
		Acute infective and toxic
		Phlegmonous
Chronic gastritis	{	Superficial
		Atrophic
		Hypertrophic
		Gastritis of the post-operative stomach

This scheme is open to criticism because it is a mixture of ætiology and morbid anatomy, and because it gives the conception of different types of chronic gastritis. My experience suggests that superficial, hypertrophic and atrophic changes can be stages and phases of a single disease process—a non-specific gastritis. The following classification is offered:

Unknown cause—Non-specific gastritis.

Unknown cause		Non-specific gastritis.				
Known cause	Exogenous gastritis	{	Mechanical	{	Bad eating habits	
					{	Post-operative dyspepsia
	Endogenous gastritis	{	Chemical	{	Pyloric stenosis, &c.	
					{	Alcohol
		{	Infective	{	Aspirin	
					{	Corrosives, &c.
		Toxic	{	Salmonella		
				{	Diphtheria, &c.	
					{	Uremia, &c.

It is important to give a full description of the gastroscopic changes and this outline is suggested:

Degree	Slight (? superficial)
	Severe
Activity... ..	Acute (active)
	Chronic (quiescent)
Position... ..	Antrum
	Body
	Fundus
	Localized or generalized
Thickness of mucosa	Normal
	Hypertrophic
	Atrophic
	Atrophic and hypertrophic
Associated changes	Hyperæmia, œdema, exudate, hæmorrhage, erosion, ulcer, polyposis

Non-specific gastritis does not seem to be a common condition. Among 337 admissions for hæmatemesis and melæna, of whom over half had been gastroscoped usually in the first week, only 7 have been thought to have an active gastritis to account for their bleeding. Attending the Dietetic Department last year at the Central Middlesex County Hospital there were 553 new patients with peptic ulcer, and 158 patients with X-ray negative dyspepsia—about a quarter had been gastroscoped and gastritis diagnosed 10 times as a cause of symptoms. The following are illustrative cases.

F., aged 39 (L. 7032).

Six months' left epigastric pain five minutes p.c. (after food). Barium meal N.A.D. Fractional test meal: Achlorhydria even after histamine. Gastroscopy showed some degree of atrophic changes in the body of the stomach and an intense inflammatory reaction with hyperæmia and excess of mucus (fig. 4). She returned six months later with two weeks' pain, and then a hæmatemesis. Gastroscopy again showed gastritis near the angulus and there was a small subacute ulcer with a red rim.

M., aged 23 (L. 8799).

One year persistent gnawing epigastric pain immediately p.c. Little alcohol and smoking. Barium meal N.A.D. Cholecystogram N.A.D. F.T.M. achlorhydria even after histamine. Gastroscopy showed extensive atrophy of the mucosa of body of stomach with an intense inflammatory reaction, most marked on lesser curvature and posterior wall with much patchy hyperæmia and excess of mucus (fig. 3).

F., aged 47 (L. 1412).

Bout of indigestion twenty years ago and slight attacks occasionally since. Six months ago onset of epigastric pain two hours p.c. Worse recently. Appetite good. Little alcohol and 10 cigarettes daily. Barium meal N.A.D. F.T.M. prehistamine achlorhydria, rising to 25 units after histamine. W.R. negative. Gastroscopy showed an acute inflammatory reaction mainly affecting the pyloric antrum, particularly the anterior wall and greater curvature. The mucosa was swollen, hyperæmic and with excess of mucus, but no definite ulceration. Six months later the patient was well.

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				Chemical	{ Alcohol Aspirin Corrosives, &c.
				Infective	{ Salmonella Diphtheria, &c.
	{	Endogenous gastritis	{	Toxic	{ Uremia, &c.

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M., aged 48 (K. 8738).

Admitted with hæmatemesis. Slight epigastric pain next day only. Three recurrent bleedings. Transfusion totalled 5,940 c.c. Gastroscopy on fifth day after bleeding had ceased showed a fine mammillated mucosa with intense patchy hyperæmia and œdema affecting the whole of the mucosa. No ulcer seen. F.T.M. showed acid curve reaching 25 units. Barium meal showed a fine irregularity of the mucosal pattern. Alcohol seldom taken. 20 cigarettes daily.

M., aged 46 (L. 9119).

Twenty years' history of remittent dyspepsia. Right epigastric pain half an hour p.c. Admitted with hæmatemesis. Gastroscopy showed atrophic changes on the anterior wall and hypertrophic changes (fig. 5) on the posterior wall and a small red-rimmed erosion near the angulus. On a subsequent admission there was an intense superficial gastritis present as well as a subacute gastric ulcer. Partial gastrectomy was performed and a high degree of chronic gastritis was found histologically. Barium meal was normal. F.T.M. showed a prehistamine achlorhydria. No smoking or alcohol.

An important discrepancy between gastroscopic and histological findings is the frequent presence of a pyloric gastritis in resection specimens, but this is seldom diagnosed with the gastroscopie (Magnus and Rodgers, 1938).

The final proof in the diagnosis of gastritis must be histological, and it is true to say that the correlation between gastroscopy and histology is not yet fully achieved. The limits of normality are not yet clearly defined either gastroscopically or histologically for it is extremely difficult to acquire normal stomachs fixed with formalin very soon after death and it is also difficult to obtain large numbers of normal subjects for gastroscopy. The whole edifice of gastritis is top-heavy and needs a broader foundation of careful description of the stomach in the adult who has been free from dyspepsia. It is possible that the pyloric gastritis found in resection specimens is actually a histological change associated with adult life for Magnus (1937) observed it in 13 post-mortem specimens in miscellaneous medical conditions and without gastric ulcer or neoplasm.

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Dr. G. R. Mather Cordiner: The radiological investigation for gastritis is based upon the study of the mucosal relief pattern, obtained by coating the mucous membrane of the stomach with a thin layer of contrast medium. By this means, variations in the pattern and consistency of the mucosal folds can be investigated and demonstrated.

The normal mucosal folds of the stomach have certain important characteristics which can be shown radiologically. The folds are of uniform thickness, they are soft and flexible and can be displaced and deformed by pressure. With gradually increasing pressure, the folds become flattened with a corresponding narrowing of the valleys between the folds. If sufficient pressure is applied, the folds can be completely smoothed out but they reappear when the pressure is released.

The radiographic changes which are seen in gastritis may be considered under four headings:

(1) *The secretory condition of the mucosal surface.*—Under normal conditions the contrast medium flows over and adheres to the mucosal surface of the stomach in a uniform manner. In gastritis, there is an alteration in the slipperiness or stickiness of the mucosal surface. This appears to be due to the character of the inflammatory exudate, probably its fibrin content. The more recent forms of gastritis have a slippery secretion and the mucosa loses its adhesive property for the opaque medium. In the more chronic lesions, the adhesive property of the mucous membrane is increased. One gets the impression that the mucosal surfaces are sticking together and that they are slowly separated from each other by the opaque medium as it flows slowly over the mucous membrane. The contrast medium sticks more firmly than usual to the mucosal surface and frequently has a fine granular appearance.

(2) *Variations in the mucous membrane autoplasmic.*—The modern conception of the gastric mucosa is that it is a plastic organ with its own autonomic motility mechanism—

the autoplasmic. The mucosal folds are not anatomically preformed structures but are produced in response to the needs of digestion. The factors which control the autoplasmic are the condition of the submucosa, particularly its fluid content, and the contraction of the muscularis mucosæ.

A mild degree of gastritis stimulates the mucous membrane autoplasmic so that an unstable and rapidly changing mucous membrane relief is obtained. This is specially noticeable in the pyloric region. As the inflammatory changes become more pronounced, the mucous membrane autoplasmic is depressed and where the inflammatory lesion is very severe, the autoplasmic is paralysed. The mucous membrane no longer appears to be capable of independent movement.

(3) *Changes in the consistency of the mucosal folds.*—Important characteristics of normal mucosal folds are their softness, mobility, flexibility and their deformation and obliteration by pressure. Pathologically altered folds show a loss of flexibility, a decrease of movement on palpation and they are less easily deformed and smoothed out by pressure and by stretching. The stiffening is comparable to that which takes place in a garment after it has been starched. This rigidity of the folds is the most important feature in gastritis and unless stiffening is present, a radiological diagnosis of gastritis is seldom justified. When a pathologically altered relief is deformed or obliterated by pressure, the same fold configuration does not appear when the pressure is released.

(4) *Changes in the mucosal pattern.*—In a large proportion of cases, the basic pattern of the mucosal relief is not altered in gastritis. The folds are broadened and swollen and there is a corresponding broadening of the valleys between the folds. Unless the swollen folds show also rigidity, they must not be interpreted as indicating the presence of gastritis. Large folds do not signify hypertrophy, a term which is only rarely justified radiologically in describing gastritis. The size of the folds is not an index of the condition of the mucosa but is a reflection of the state of the submucosa and of the muscularis mucosæ. The continuity of the pathologically altered folds is usually disturbed and the folds are invariably diminished in number and they do not have a uniform calibre. A rare finding is the presence of small polypoid elevations of the mucosa, giving rise to the "corn-cob" relief. These small rounded elevations represent a true hyperplasia of the mucosa.

A radiological diagnosis of gastritis is possible when the mucosal relief is abnormal and is accompanied by rigidity of the folds. A diagnosis of hypertrophic gastritis is only possible in the presence of a polypoid hyperplasia of the mucosa. There are no characteristic findings which enable the radiologist to diagnose atrophic gastritis.

Dr. P. E. Thompson Hancock: Of the various types of gastritis that are described clinically, histologically and gastroscopically only two, apart from the acute forms, have a recognizable syndrome, namely, alcoholic gastritis and chronic diffuse atrophic gastritis. Alcoholic gastritis has long been recognized and is familiar, though of necessity it is now on the wane. Chronic atrophic gastritis can, I believe, often be recognized. The patient is usually in the third or fourth decade and complains of fatigue, listlessness, anorexia and loss of weight. Abdominal pain is not usually severe, dull epigastric discomfort, especially after meals, being the usual complaint, but sometimes a day or two of quite sharp epigastric pain may occur—this coincides with the gastroscopic recognition of an acute erosion. The abdominal discomfort is not alleviated by alkalis. Nausea and vomiting are exceptional. On examination there may be some anæmia, but there is little or no epigastric tenderness. If with this clinical picture there is no radiological evidence of gastric abnormality, and no free acid is found in a fractional test meal, a diagnosis of chronic atrophic gastritis is justifiable. Some gastro-enterologists, however, have written careful accounts of the syndromes associated with other forms of gastritis, a particularly full account of several of these is given by Schindler in his book on gastroscopy, but I have not myself been able to confirm these clinical pictures. This is unfortunate as the two types that I have just mentioned form but a small part of the cases of gastritis. Chronic catarrhal gastritis is the commonest form, but this, in my opinion, has no recognizable syndrome and probably is often symptomless.

The radiological diagnosis of gastritis.—Dr. Mather Cordiner has described the mucosal relief technique as applied to gastritis. In my experience, however, radiology has not helped in the diagnosis of gastritis and has often in fact been definitely misleading. I

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An important discrepancy between gastroscopic and histological findings is the frequent presence of a pyloric gastritis in resection specimens, but this is seldom diagnosed with the gastroscope (Magnus and Rodgers, 1938).

The final proof in the diagnosis of gastritis must be histological, and it is true to say that the correlation between gastroscopy and histology is not yet fully achieved. The limits of normality are not yet clearly defined either gastroscopically or histologically for it is extremely difficult to acquire normal stomachs fixed with formalin very soon after death and it is also difficult to obtain large numbers of normal subjects for gastroscopy. The whole edifice of gastritis is top-heavy and needs a broader foundation of careful description of the stomach in the adult who has been free from dyspepsia. It is possible that the pyloric gastritis found in resection specimens is actually a histological change associated with adult life for Magnus (1937) observed it in 13 post-mortem specimens in miscellaneous medical conditions and without gastric ulcer or neoplasm.

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Dr. G. R. Mather Cordiner: The radiological investigation for gastritis is based upon the study of the mucosal relief pattern, obtained by coating the mucous membrane of the stomach with a thin layer of contrast medium. By this means, variations in the pattern and consistency of the mucosal folds can be investigated and demonstrated.

The normal mucosal folds of the stomach have certain important characteristics which can be shown radiologically. The folds are of uniform thickness, they are soft and flexible and can be displaced and deformed by pressure. With gradually increasing pressure, the folds become flattened with a corresponding narrowing of the valleys between the folds. If sufficient pressure is applied, the folds can be completely smoothed out but they reappear when the pressure is released.

The radiographic changes which are seen in gastritis may be considered under four headings:

(1) *The secretory condition of the mucosal surface.*—Under normal conditions the contrast medium flows over and adheres to the mucosal surface of the stomach in a uniform manner. In gastritis, there is an alteration in the slipperiness or stickiness of the mucosal surface. This appears to be due to the character of the inflammatory exudate, probably its fibrin content. The more recent forms of gastritis have a slippery secretion and the mucosa loses its adhesive property for the opaque medium. In the more chronic lesions, the adhesive property of the mucous membrane is increased. One gets the impression that the mucosal surfaces are sticking together and that they are slowly separated from each other by the opaque medium as it flows slowly over the mucous membrane. The contrast medium sticks more firmly than usual to the mucosal surface and frequently has a fine granular appearance.

(2) *Variations in the mucous membrane autoplasmic.*—The modern conception of the gastric mucosa is that it is a plastic organ with its own autonomic motility mechanism—

changes are physiological rather than pathological, influenced by an extra-uterine mechanism and not related at all to local inflammation. Again, if one could obtain only a distant and fleeting glimpse of the skin, it might be difficult to say whether the subject was blushing or suffering from a dermatitis.

Our understanding of gastritis will be advanced perceptibly when it becomes possible safely to perform biopsy upon the gastric mucosa and to obtain a specimen of sufficient quality to allow histology of the living mucosa. The biopsy attachment to the flexible gastroscope introduced by Kenamore does not so far fulfil these conditions.

Meanwhile certain conclusions can be drawn from a combination of gastroscopic and secretory studies. If maximal secretion of any given stomach is to be obtained, both phases, chemical and nervous, of normal secretion, require stimulation. Histamine, acting directly on the mucosa, is the most powerful stimulant of the chemical phase, while intravenous insulin, leading to hypoglycæmia, which in turn stimulates the vagus nucleus in the medulla, induces a strong flow of nervous juice. Thus, a summation of chemical and nervous secretion can be obtained and measured, while the mucosa can be inspected with the gastroscope at the height of secretion. In the normal, the mucosa becomes hyperæmic and exudes a clear fluid which trickles downwards in rivulets between the folds to form a pool on the greater curve (the patient lying on his left side). The secretion rate averages 2.5 to 3.5 c.c. per minute and free HCl concentration 100 to 120 c.c. In subjects showing the gastroscopic appearances labelled hypertrophic gastritis, the highest concentration of free HCl (160 to 200 c.c.) and highest rate of secretion (6 to 6.5 c.c. per minute) is seen.

Now, it is not usual to associate inflammation with enhanced function and I would submit that these observations suggest that some cases at least of so-called hypertrophic gastritis are in reality merely a physiological mucosal hyperactivity. In subjects showing the gastroscopic appearances labelled atrophic gastritis there is pallor of the mucosa with great diminution of secretory function (complete achlorhydria: secretion rate less than 1 c.c. per minute). This combination, although perhaps compatible with a very chronic low-grade inflammatory process, is I think more suggestive of a degenerative process and certainly in some cases a degree of regeneration with some return of function can occur spontaneously after some months. I would therefore suggest that the time has come to abandon the term chronic gastritis and to use instead purely descriptive terms, e.g. mucosal hypertrophy, mucosal atrophy, or mucosal hyperæmia.

Sir Henry Tidy: The experienced gastroscopists who have spoken to-day agree as to the rapidity with which appearances of the gastric mucous membrane can change. This is an advance on earlier views which held that variations from what was considered normal were permanent. The work of Wolf and Wolff referred to by Dr. Izod Bennett affords proof of the rapidity with which the gastric mucous membrane can change as the result of comparatively slight physical and nervous stimuli. It is in agreement with these rapid changes that it is difficult to correlate the appearance of the gastric mucous membrane with the symptoms. Gastroscopy caused some difficulty in the early days of the war. There was a flood of dyspeptic complaints, the symptoms showing no characteristic differences. Gastroscopy would reveal normal mucous membrane in one, and what was held to be a pathological condition in another. The question arose whether these differences justified different methods of disposal. Should one man be discharged and another return to his unit on the strength of the gastroscopy although symptoms and history were identical?

Dr. J. Jacques Spira: The following is a simple but comprehensive classification of chronic gastritis which may help to clarify the conception of gastric pathology.

A. *Direct causes* (local manifestations).—Inflammatory processes associated with increased acidity and chronic peptic ulcer, and subject to immediate relief and cure by the removal of the offending agent.

(1) *Chronic superficial or catarrhal gastritis* produced by mild repeated irritation. (a) Mechanical, thermal, chemical factors (alcohol, tobacco, drugs, highly spiced foods, &c.). (b) Swallowing of purulent material (chronic infections of post-nasal, gingival, pulmonary, intestinal origin).

have gastroscoped many patients in whom a diagnosis of gastritis was made on the radiological appearance of enlarged and irregular folds, and have found that in most of these cases the folds were normal large folds with no evidence of inflammation. I have been fortunate enough to work with several radiologists who have taken great interest in the correlation of the radiological and gastroscopic appearances, and they have come to see most of their patients gastroscoped. They now very rarely make any pronouncement about gastritis, confining their comments to the size of the gastric rugae.

The gastroscopic diagnosis of gastritis.—There are many pitfalls for the gastroscopist. At the American Medical Association Meeting in 1938, in a discussion by the Gastroenterological Section on the subject of gastritis, I was able to record then 50 cases which I had gastroscoped and which had had gastric resections afterwards. In many of these cases I had found extensive gastritis of one type or another. I had had serial sections cut of these stomachs after careful fixation and, although most of them showed histological evidence of gastritis, the types did not correspond with the gastroscopic appearances. Particularly was this true of the so-called hypertrophic type, which I frequently diagnosed, but which I found was rare histologically, and which I seldom diagnose now.

I myself have made just over 1,400 gastroscopic examinations, and find that I have made a diagnosis of gastritis in about 21% of these cases; but whereas in my first 300 cases I diagnosed hypertrophic gastritis 18 times, or 6% of the cases, in my last 300 instrumentations I have only diagnosed it twice, or 0.66%. This is, I believe, mainly due to the fact that the normal stomach has a far wider range of size and distribution of folds and degree of visibility of the area gastrica than was formerly recognized, and the criterion of the diagnosis of hypertrophic gastritis must be the presence of definite evidence of inflammation. In all other forms of gastritis I find that my percentage frequencies are fairly constant throughout the series.

Conclusion.—Gastritis is rarely diagnosable as a clinical syndrome, and gastroscopy is the only investigation that enables a positive diagnosis to be made. The gastroscopic diagnosis, however, is not infallible, the tendency being to diagnose gastritis too frequently owing to insufficient allowance being made for the great variations that normally occur in the gastric mucosa.

Dr. Morton Gill: Two outstanding observations concerning gastritis have been made during the last hundred years.

The first was Beaumont's observation that Alexis St. Martin's mucosa became congested temporarily after over-indulgence in alcohol and that this change was accompanied by a queasy sensation in the epigastrium, nausea and loss of appetite. Thus it was shown that acute but temporary mucosal changes, called acute gastritis, could follow the ingestion of a poison and that these changes ran *pari passu* with symptoms, also temporary.

The second series of observations, made by Wolf and Wolff on their now famous subject, Tom, have shown that the gastric mucosa can reflect mental changes to an extraordinary degree. Thus, with anxiety and resentment there is swelling and congestion, increased motility and increased secretion of HCl, a physiological hyperactivity associated with increased vascularity. These changes are accompanied by symptoms of discomfort referred to the epigastrium. Fear on the other hand, produces pallor of the mucosa accompanied by a diminished secretion of acid. From these observations it follows that gastritis may be the result of direct damage to the mucosa by a local irritant but that equally, visible mucosal changes, initially vascular, in the nature of alterations in blood flow, may be of central origin. Thus, when we come to the radiological or gastroscopic diagnosis of chronic gastritis, based upon mucosal changes and pretending to the explanation of symptoms of chronic dyspepsia, it is at present difficult, if not impossible, to be certain as to whether some at least of the mucosal changes may not be an expression of anxiety on the part of the patient, either of the examination itself or of its results.

This is not to deny the existence of chronic inflammatory lesions affecting the stomach—the work of Faber and others is sufficient evidence—but it becomes a difficult thing to say whether in a given case, the mucosal changes found are of central or local origin, temporary or permanent and whether, in any case, they are the cause of the patient's symptoms.

One might perhaps draw an analogy with endometritis, a diagnosis commonly made in the past, but largely discarded once it was realized that a wide range of endometrial

Mr. C. Jennings Marshall: The existence of controversy on the subject of gastritis seems clear indication that insufficient attention has been paid to the fundamental principle of correlating symptoms with demonstrable pathology; in this is intimately bound up the question of how gastric disease in general produces symptoms and how gastric symptoms may arise without gastric disease. We must above all distinguish between the effects on the sensorium produced by purely mucosal disease and those of implication of the musculature; innumerable writings have stressed, rightly I feel, the overwhelmingly important part played by muscular involvement and the relative silence of the mucosa—that considerable gastritis, convincingly demonstrable, frequently exists without symptoms indeed should occasion no surprise.

Varieties of gastritis.—For the purpose of this discussion it is convenient to ignore detailed reference to acute cellulitis (phlegmon) of the stomach and to the effects of corrosives. Chronic gastritis occurs both as a primary gastric disease and as one secondary to other gastric conditions.

Secondary chronic gastritis.—This arises in two ways: from any chronic obstruction and as a complication usually local, of an ulcer, simple or malignant.

Obstructive.—Stenosis of any canal in which organisms live results in increased bacterial proliferation with inflammatory changes, e.g. the diarrhoea-producing colitis above a carcinoma coli. Congenital stenosis of the pylorus produces a mucosal gastritis which leads to oedema of the hypertrophied pylorus and so to the classical delayed total obstruction; microscopy of portions of the muscle removed at a pylorotomy clearly shows this, the pyloric lymph glands show hyperplasia; systematic preliminary gastric lavage greatly reduces the gastritis and has largely eliminated the acute gastrogenous diarrhoea so often a dangerous sequel to pylorotomy before the adoption of this procedure.

The obstruction from fibrosis and oedema in juxtapyloric ulceration or from carcinoma similarly produces a generalized gastritis, at first superficial, later becoming interstitial with hyperplasia, only in very prolonged cases resulting in mucosal atrophy and achlorhydria. It is only uncommonly that this condition is irrecoverable after lavage or relief of the obstruction surgically; it is unsafe to assume an immunity from stomal ulceration after gastrojejunostomy unless considerable time has been spent in observing the reaction to treatment. The obstructive gastritis associated with a carcinomatous ulcer owing to the infection of the breaking-down surface is of a more severe and rapidly progressive type and is responsible for one type of achlorhydria seen in cancer of the stomach. It still seems to be little known that such achlorhydria is frequently recoverable with measures aimed at reducing the infection, e.g. lavage and frequent small feeds. Local circum-ulcerous cellulitis implicating all the gastric layers is the cause of all the symptoms of peptic ulceration apart from perforation and massive hæmorrhage, and also of the majority of stomal troubles in gastrojejunostomy. The case is comparable to the flares of cellulitis around an ulcer of the leg. The minor persistent hæmorrhage which is the basis of occult blood in the feces comes from the intensely congested mucosa, not from the ulcer surface as is so commonly taught; the crater seen radiographically is produced mainly by a filling defect due to projection into the gastric lumen of the oedematous mucosa and submucosa. With the subsidence of the cellulitis the X-ray signs—crater, rigidity, &c.—disappear completely leaving an asymptomatic epithelial defect which, gastroscopy shows, heals extremely slowly even with the optimum medical treatment. The symptoms of cancer of the stomach are also due largely to inflammatory oedema affecting the musculature—cancerous infiltration of musculature without infection (e.g. in leather-bottle stomach) produces little if any pain; treatment effective in reducing infection (lavage or short circuit) notably reduces symptoms. Similar relief of pain is found in the treatment of cancerous ulcers elsewhere, e.g. oral cleansing in cancer of the tongue.

The instances cited of local gastric cellulitis support strongly the contention that muscular involvement is the main basis of gastric pain. Where generalized mucosal gastritis exists as the result of obstruction, it produces little or no symptoms *per se*. A pyloric obstruction though accompanied by severe hyperblastic gastritis usually has the symptoms of obstruction alone—distension, colic, vomiting. Finally it has to be observed that the gastritis here is no mere hypothesis—it is a disease with proof based on naked-eye and microscopic evidence: gastric tissue placed immediately in a fixative after operative removal is not subject to these inevitable post-mortem autolytic changes which make such observations untrustworthy to a large extent. The most serviceable classification of mucosal gastritis remains that of Schindler—superficial, hypertrophic and atrophic—the last two being interstitial in type with leucocytic infiltration, lymphoid aggregations and

(2) *Chronic hypertrophic gastritis* produced by *severe* repeated irritation. (a) Marked effect produced by regurgitation of bile into the stomach. (b) Persistence of chronic superficial gastritis. After gastro-intestinal anastomosis.

B. Indirect causes (systemic manifestations).—Degenerative processes associated with decreased acidity and gastric carcinoma, and subject to regeneration with appropriate substitution treatment.

Atrophic gastritis (atrophy of the gastric mucosa).—(1) *Primary factors* associated with deficiency diseases. Simple microcytic anemia. Addisonian anemia. Subacute combined degeneration of the cord. (*A process of glandular degeneration.*)

(2) *Secondary factors* associated with other pathological conditions. (a) Following 20% of cases of virulent acute gastritis (Schindler). (*A process of glandular destruction.*) (b) In pyloric stenosis. After intensive alkaline treatment. Achlorhydria of old age. (*A process of glandular exhaustion.*)

Mr. N. C. Tanner: In gastroscopy one can, broadly speaking, divide the gastric mucosa into three: thick, medium, thin. In the absence of gastritis the gastric acidity appears to vary directly with the thickness, and there is a general tendency to thinning of the mucosa and lowered acidity in later life. On these basic types inflammatory, ulcerative or neoplastic lesions may be set. In a thick mucosa one can normally see areæ gastrice which on viewing obliquely and close up appear knobbly—the so-called cobblestone-appearance. In the thinner mucosa there is a loss of the mucosal anatomic pattern and increasing transparency—the latter appearance being accentuated by gastric distension or by pallor of the mucosa.

The earliest so-called inflammatory changes, congestion, excess of mucus or catarrhal exudate are frequently seen, appear to be readily provoked and are most easily seen in the thick mucosa where they give rise to the appearance often called "hypertrophic gastritis". Such changes are often seen in absence of symptoms or in patients in whom other adequate causes for the symptoms are found. These appearances may often be the results of momentary stimuli.

True polypoidal changes in a thick mucosa are rare in my experience. The changes often described as hypertrophic gastritis I would call normal, or in the presence of marked inflammatory change I would call gastritis in a thick mucosa. True mucosal polypi in a thick mucosa I have only seen twice and eight times in a thin mucosa, but these changes should probably be regarded as neoplastic. An appearance of polypoidal hyperplasia may be simulated by œdema and congestion due to gastric stasis in the thick gastric mucosa associated with duodenal ulcer. I believe a large number of those cases of periodic dyspepsia diagnosed gastroscopically as hypertrophic gastritis are really duodenal ulcers which have escaped the radiologist's attention.

In evaluating the mucosal signs "pigment spots" appear to be often the result of the trauma of a previous test meal or of the introduction of the gastroscope. A congested patch with pale adherent mucus may be produced by placing the hot lamp of the gastroscope against the mucosa for a few moments.

We would do well to compare the gastric with the lingual mucosa, despite their histological differences. Although a congested coated tongue such as may follow over-indulgence in smoking, spirits or curry may be sore, more often a coated tongue is symptomless and consistent with perfect health, or may be a sign of disorder elsewhere, not necessarily in the digestive tract. To my mind the same applies to the milder "inflammatory" changes in the stomach.

I have recently investigated the gastroscopic diagnoses made at St. James' Hospital between the end of 1939 and the end of last year. In a series of 2,200 gastroscopies performed on 1,730 patients there were 631 gastric ulcers, and 267 had varying degrees of "inflammatory" change, but only 65—under 4%—had reasonably well-marked or chronic gastritic changes which might be considered a possible cause for the symptoms. Certainly I do not find a pure gastritis in the absence of marked gastric obstruction, gastric ulcer or neoplasm are nearly as common a condition as gastric ulcer—in fact about one-tenth as common.

Section of Surgery

President—Sir JAMES WALTON, K.C.V.O., M.S.

[November 1, 1944]

DISCUSSION ON TREATMENT OF DUODENAL ULCER

Sir James Walton: Since 1905 I have carefully indexed and filed the literature on the subject of peptic ulceration, and have always been puzzled by the fact that whereas the findings of most surgeons in this country and the United States were in accord with my own, most of the pre-war experiences of Continental surgeons were entirely contrary to mine. Nevertheless there appears to be an increasing number of younger surgeons who are following their teaching. I believe that there is a growing danger to-day that surgeons may revert to the mediæval custom of accepting the written word without question and of falling away from the Hunterian tradition of finding the truth for themselves.

It is essential for every surgeon to have a well-organized follow-up department in which he can carefully and conscientiously study his own results so that he can change his methods if these results are not satisfactory. My own hospital with wide vision provided me with what I believe to be the first clinic of this sort in Great Britain immediately after the last war. My present views are based on that twenty-five years follow-up. Since technical surgery is an art, no man is entitled to say that one form of treatment is alone correct. All that he can say is that it gives the best results in his own hands; others may find different methods more suitable.

In considering the selection of cases for surgical treatment I think that physicians and surgeons to-day are in agreement that the one indication for surgical interference is the failure of medical treatment. Even the presence of stenosis, or hæmorrhage or even of perforation is in a sense evidence that the condition has not been cured medically. It must, however, be realized that the standard of cure will vary with the social position of the individual patient. A man in comfortable circumstances may keep free of symptoms and be apparently cured on a diet and in a sheltered life impossible for a working man. A stevedore for instance may have to make his midday meal off bread and cheese and an onion and perhaps a bottle of beer, and would find himself but ill-equipped with a bowl of Benger's Food.

As regards the operative technique for uncomplicated cases, the decision in this country lies in the majority of cases between posterior gastro-enterostomy and partial gastrectomy. Local excision with plastic procedures upon the pylorus may be the method of choice for a few cases, but has not obtained so wide a vogue as in some other countries. The choice of one or other of these two procedures is of course entirely dependent upon the frequency of gastrojejunal ulceration after posterior gastro-enterostomy. Many reports have been published by Continental surgeons and some from the United States showing an incidence

fibrosis extending deeply among the glands which show in the former case varying degrees of hyperplasia, in the latter aplasia, metaplasia, heterotopia particularly in the pyloric area, thinning of the mucosal layer and avascularity. The hyperblastic type is subject frequently to mammillary projections generalized throughout, and to thickening and œdema of the submucosal tissue; in some cases there are polypi. These are of particular importance from the point of view of radiological diagnosis; it is only when gross macroscopic changes of this order are present that significant alterations in the X-ray appearances are to be expected. Superficial gastritis is clearly not recognizable, atrophic may only be suspected; only when fixed, rigid, coarse, mucosal patterns are seen can the diagnosis of hypertrophic gastritis be made. In some cases such mucosal folds and polypoid formations, particularly in the pyloric region, cause persistent filling defects and arouse the suspicion of cancer.

Primary gastritis.—The consideration of primary gastritis has been placed second because it is the study of the secondary forms that has provided us with the pathological and symptomatic knowledge of the condition. Cautious gastroscopic recognition may be made in two ways: Allowance must be made for considerable variations in the appearance of normal stomachs and supposedly gastric symptoms must not be linked with even clearly recognizable changes unless these are of such a type as might reasonably be expected to produce the symptoms. In the case of the psychotic, while admitting the importance of excluding organic disease, it must be remembered that investigations such as X-rays, test meals or gastroscopy serve but to "fix" a gastric neurosis. Indeed many gastroscopists, with considerable justification, place neurosis on the list of contra-indications. The reaction of such patients to gastroscopy is almost diagnostically unco-operative and resistive.

Many authorities have insisted on gastritis as a precursor of cancer; yet it is certain that the symptoms of the cancer arise in the vast majority of cases out of a blue sky; while secondary gastritis is an almost invariable accompaniment of cancer, mucosal changes of the nature of polypoid formation, glandular heterotopia and metaplasia are evidence of disease much too prolonged in nature to be accounted for in this way. If one accepts the theory therefore there is the inevitable conclusion that mucosal gastritis with gross structural changes may be symptomless. Such gastritis, unequivocally proved from the microscopic point of view, is found in a high proportion of post-mortems in all persons over the age of 40 with a similar inference to symptomatology.

Symptoms.—*Hæmorrhage* is an occasional manifestation occurring from superficial erosions; it may be brisk but is never prolonged or severe in such cases; rarely there is a generalized oozing from the whole stomach surface, the old "gastrostaxis", analogous with that in some cases of infective colitis.

Anorexia in severe interstitial gastritis with achlorhydria is common and clears up with treatment.

Pain sometimes colicky, sometimes burning, usually vaguely dyspeptic only, sometimes with nausea and vomiting, arises in connexion with gastritis affecting the prepyloric region. it reacts poorly if at all to ulcer regimen. Frequently the radiologist reports spasm in the pyloric region, often with thickened mucosal folds. Gastroscopy here is conclusive, showing swollen folds, even polypoid changes—there is generalized gastritis also as a rule. Clearly the mechanical interference with the prepyloric musculature is responsible for the symptoms. Experience of some two thousand gastroscopies during the past seven years has shown gastritic changes in a high proportion—some 50% of cases over the age of 40; unless some such appearance is found in the antrum, it is unwise to attribute symptoms to the gastritis, the rest of the mucosa is silent, and the view that gastric pain is muscular in origin is fully justified.

with this view I am in accord, that such an operation would generally be too severe a strain upon so ill and enfeebled a patient. The method of ligating arteries running to the ulcer, which is so often advocated, has in my experience generally been a failure, for the arterial anastomosis is so free. The ulcers are often so large that any form of local excision is impracticable. In many cases of duodenal ulcer the anterior wall of the duodenum may be so widely invaginated by a running mattress suture that the lumen is entirely occluded and the anterior wall pressing firmly upon the ulcer safely controls the hæmorrhage. The operation is completed by the performance of a posterior gastro-enterostomy. In other patients, however, the duodenal wall is so indurated that invagination is impossible. Under these conditions and with all large gastric ulcers I believe that the safest and most satisfactory method consists of opening the viscus, underpinning the bleeding vessels and suturing the ulcer crater with interrupted mattress sutures. In the case of the duodenum the opening in the anterior wall should be embedded after suture and a posterior gastro-enterostomy performed.

These are simply my present opinions which are based upon a considerable amount of most carefully controlled experience.

Mr. C. Jennings Marshall: The primary treatment is medical, the essential of which is physical and mental rest, the one common factor of varied "successful" regimes; as we see in treatment of severe bleeding, symptoms disappear as rapidly with water-fasting as with any drug and diet system. But it is vital to distinguish between cure of symptoms and cure of the ulcer which persists long after disappearance of X-ray signs and occult blood in the focus. The hydrochloric figure by no means represents the peptic activity and is unreliable in estimating progress and prognosis. While certain food abstinences relieve or minimize symptoms, they cannot be relied on to secure freedom from recurrence; nevertheless only about one-sixth of the cases need surgical intervention. Perforation rarely recovers without surgery and recurrent perforation calls for radical measures, as does recurrent bleeding; individual massive hæmorrhages are primarily to be treated by functional rest and leaving the blood-pressure at the lowest level warrantable; only after four or five days, when it is clear that arrest is not obtained, must we consider surgery; massive transfusion then enables us to deal with a very difficult technical problem. Obstruction is partly fibrous, largely œdematous, the latter recovers with rest, lavage or drainage, and oral hygiene. Before the stomach is emptied the chloride balance must be attended to or tetany may be precipitated. Obstruction is accompanied by mucosal gastritis, first superficial then interstitial; only late and rarely does this become atrophic; the achlorhydria often seen is relieved by lavage and drainage, a high secretory figure being resumed, so that a single observation is unsafe for predicting freedom from stomal trouble after anastomosis; the gastroscope is useful here, a hyperplastic gastritis renders the outcome of gastro-enterostomy dubious. Undoubtedly a proportion, less than a half, of gastro-enterostomies are very satisfactory. Progressively frequent and more severe relapses leading to invalidism constitute the remaining surgical indication. *Gastrectomy* is becoming less and less dangerous with adequate preparation—oral hygiene, lavage, and attention to Hb. and blood colloids, breathing exercises, muscular and vascular tonus. Subjects with a good Moots-McKesson ratio are suitable for spinal analgesia; bad risks need local and splanchnic blocking with cyclopropane or gas and oxygen—prolonged anoxæmia leads to serious post-operative myocardial danger. The heresy that owing to the perfection of modern anaesthesia it does not matter if the operation takes two or three hours is strongly to be deplored, though speed must never be obtained by roughness or skipping technical details; three hours' anaesthesia alone, without operation, would have an appreciable mortality. The stomach should be resected from high on the lesser curve to a little below the spleen; in deeply penetrating and extensive duodenal ulcer the stomach may be divided $1\frac{1}{2}$ in. proximal to the pylorus but it is essential to enucleate the antral mucosa—I have practised this since 1928 in cases where removal of the ulcer inevitably leads to anxiety about infective morbidity, and danger to pancreatic and bile ducts; the possibility of leakage calls for precautionary drainage down to any dubious stump. Gastroduodenal anastomosis is permissible only when there is no gross stenosis or infection—in any case the duodenum has *not* shown itself a satisfactory recipient of gastric juice! The Polya-Moynihan operation is frequently followed by "dumping" into the jejunum, and duodenal reflux—the opening should be little larger than gut calibre and the proximal jejunum hitched up to the gastric suture line an inch or so above the union. Antecolic anastomoses are functionally sound and in the uncommon event of stomal troubles lessen the difficulties, if future operation is needed, of the short proximal loop, adhesion to the middle colic artery and implication of the transverse colon. Stomal

of 30 to 35% and I cannot help but feel that many of our surgeons have been unduly influenced by these reports, which may deal with conditions dissimilar to those in this country, and therefore always perform a partial gastrectomy. My reason for this belief is that in my carefully controlled follow-up results my incidence has always been about 4% and these results have been constant from the time when my cases of duodenal ulcer numbered 200 until the present when they total considerably over 1,000. Moreover, although partial gastrectomy does reduce the acidity to a greater degree it does not entirely remove the danger of this complication, for in my own series of 176 gastrojejunal ulcers a partial gastrectomy had been previously performed in 12. There can be no doubt that of the two operations partial gastrectomy is the more severe. It is true that many series have been published with a very low mortality but the operations have been performed by those exceptionally skilled in the technique, and if it be generally used there is no doubt that the death-rate would vary between 5 to 10% whereas with gastro-enterostomy it should not be more than 1%. My routine custom therefore is to treat duodenal ulcers by posterior gastro-enterostomy, whether or no they be causing stenosis, and to reserve the partial gastrectomy for the 4% that have developed a gastrojejunal ulcer. Nevertheless it is my custom to try and determine the cases which are likely to develop a gastrojejunal ulcer and in them to perform a primary gastrectomy. Increasing knowledge has, I think, done much to help us to distinguish these cases. Those in whom the ulcer has started early in life and those with an unusually high acidity are probable candidates. Mr. Hermon Taylor has also shown that the presence of a hyperplastic gastritis as revealed by the gastroscope is a danger signal in such cases. My custom is to perform a partial gastrectomy for these cases. From time to time my selection of the form of gastrectomy has varied considerably. At the present time my preference lies in the end-to-end gastroduodenostomy known as the Billroth I operation, as it more closely approximates to the normal anatomy and in my experience seems to cause less operative disturbance, but if the ulceration is extensive or the duodenum widely stenosed the Polya method is selected and gives very good results. I am also convinced that the modern tendency to divide the duodenum beyond the ulcer, if the Polya operation or one of its varieties is used, is unnecessary and adds to the risk. If the duodenal stump is securely closed any area of active ulceration that may be left in the blind stump will always heal.

The surgical treatment of perforation.—Perforated ulcers are chronic lesions and therefore it is possible that simple suture may not lead to a permanent cure. This fact can be verified by anyone in the post-mortem room. In my own practice alone there have occurred 62 cases where an operation has been required for an ulcer recurring or persisting after a previous simple suture for perforation. It is rather remarkable that whereas in Russia and the Scandinavian countries the tendency is towards more radical steps, many of the cases being treated by immediate gastrectomy, in this country the accepted teaching is to do no more than a simple suture. Our first duty is to save life and the surgeon having but few opportunities of operating on these cases will most often accomplish this by simple suture. If one or two mattress sutures are used a firm closure can nearly always be brought about and reinforcement with omentum is unnecessary. My own view also is that to-day there is a dangerous dogmatism in denying the use of drainage. A suprapubic drain can never do any harm, and although many cases do well without it I have seen a number of examples of pelvic and subphrenic abscess which might have been so prevented. A case that has recovered with simple suture may recur and therefore must be carefully watched in a follow-up department and not sent away as cured. So many recur that in spite of all statements to the contrary, I am still convinced that a surgeon with wide experience is justified, in early cases, in performing a gastro-enterostomy at the first operation and my own figures have shown that the mortality is not increased thereby, if a wise discrimination is made.

The treatment of hæmorrhage.—Even the published mortality of cases treated medically, varies from 4 to over 50% and therefore each surgeon will have to formulate his treatment upon the results of his own experience. At the present time my own practice is to have all cases, whether due to acute or chronic ulceration, treated medically and only to operate if both the physician and myself feel that a second hæmorrhage is probable and if it occurs will be fatal, or if the hæmorrhage has already occurred and the patient has survived.

If an operation be undertaken a blood transfusion must always be given, being only commenced immediately before the operation is started and continued as a drip transfusion after the operation. In theory undoubtedly the most satisfactory method of control would be the performance of a partial gastrectomy but the majority of surgeons feel, and

Sir Henry Tidy: Not only are there definite differences in the character of peptic ulcer between this country and the Continent, but there are also differences between London and England and Scotland. In London gastric ulcer is considerably commoner than duodenal ulcer at the present time, but in Scotland duodenal ulcer is much commoner than gastric ulcer. There are also differences in the incidence of the two types of ulcers in various social classes. These differences would repay careful study.

Our views on gastric pathology need to be revised, especially in view of the work of Wolf and Wolff. They found that they could produce chronic gastric ulcer in four days and heal it in five days. The position is the same for gastritis. Gastroscopists now recognize the rapidity with which the gastric mucous membrane can change.

It is of importance that the relative merits of medical and surgical treatment for peptic ulcers should be discussed from time to time, for both are changing. Surgeons often appear to be satisfied that medical treatment has failed when the treatment followed would not have satisfied a physician. When a first course of medical treatment fails, a second course is often successful. Probably the patient pays more attention to the after-treatment, which is at least as important as the initial treatment.

Severe hæmorrhage as an indication for surgery must be considered in the light of recent work. Blood transfusion has been carefully standardized by Dr. Izod Bennett and his associates at the Middlesex Hospital since the introduction of the drip method by Marriott and Kekwick. Deaths from hæmorrhage are rare under the age of 40, and very rare under 35. Even at later ages deaths from hæmorrhage are usually associated with complications which exclude surgery. The most difficult cases are those of recurrent hæmorrhages with no previous symptoms.

Professor C. A. Pannett said that undoubtedly a number of patients were cured of their duodenal ulcers by medical treatment, but he was astonished to hear an experienced surgeon state that uncomplicated intractable duodenal ulcer was a medical disease. By a suitable operation such patients were transformed from wretchedly miserable complaining men to persons with a rosy outlook on life. It was necessary to take away the affected part of the duodenum with a large piece of stomach. The duodenum must be dissected free to a point beyond the ulcers so that healthy duodenal wall was available for closure. Many years ago von Eiselsberg showed how frequently a gastrojejunal ulcer developed if the pylorus were left.

The stomach should be cut across at a point where the branches of the gastro-epiploic artery rather suddenly became widely spaced. He had given up the Billroth I anastomosis because the results after it were not so good as after an operation of the anterior Polya type. He attributed this to the diminished mobility of the stomach that the former operation imposed. After such an operation in a large majority of cases the patient could eat any kind of food in three months, could eat meals of ordinary size in twelve months, and in fact became normal in that he had not to think of his digestion and was not indeed aware of the digestive processes taking place within him.

Mr. Hermon Taylor said he was not so much concerned with the treatment of acute complications, as with the situation which developed when a patient found himself getting worse and worse pain and losing more and more time at his work, in spite of all he could do in the way of conservative treatment. It was this type of patient that was referred for operative treatment, but the problem was which operation was to be performed, a partial gastrectomy or a gastro-enterostomy. There was no question that the former was much the more extensive and dangerous operation, but many surgeons had come to adopt it as a routine because of the incidence, about 25%, of anastomotic ulceration after gastro-enterostomy. It was true that when applied indiscriminately the results of the latter were quite unpredictable, the operation in some being followed by complete and permanent relief of symptoms, but in others serving merely to aggravate them. What was wanted was a means of preoperative segregation of the minority of potential failures of gastro-enterostomy, reserving partial gastrectomy for these, while performing gastro-enterostomy on the majority. Although the test meal was of some help it was too unreliable for this purpose, but the speaker had used a gastroscopic method with some success, which he wished to present to the meeting.

troubles after gastro-enterostomy—ulcer or, much more commonly, gastric cellulitis—may be treated by "restitution" if there be no duodenal stenosis or ulcer. Without great medical care, however, there is great tendency to relapse of ulceration. If gastro-enterostomy is performed to the great curve, antecolically, and transomentally with a generous proximal loop, stomal ulcer loses most of its terrors from the point of view of any future operative treatment.

Dr. Horace Evans: The diagnosis of duodenal ulceration is in most patients relatively easy, and confirmation by X-ray satisfactory. In some instances, however, the history may be quite atypical—particularly when the condition occurs in women; and a typical history may be deceptive. The frequency with which complications such as hæmorrhage, perforation and even stenosis occur in patients who have minimal symptoms of indigestion is surprising—though no doubt in some this is due to the ulcer being of a more acute type. This type of ulcer, or superficial erosion, may heal with little residual deformity and so reveal no X-ray change very soon after a hæmorrhage.

I am doubtful of the value of test meals, over which an incredible amount of time appears to be wasted. A test meal is only of real diagnostic value in cases of pernicious anæmia, carcinoma of stomach and chronic gastritis. High acid curves are commonly associated with a duodenal ulcer, but may occur without, and the converse is also true.

The treatment of duodenal ulcer remains eminently unsatisfactory.

The most satisfactory basic treatment is essentially "medical", surgery being a useful aid in selected cases. Of course, in certain instances, surgery is essential, e.g. perforation, pyloric obstruction, chronic perforating or adherent ulcers, and perhaps in certain rare examples of hæmorrhage in older patients. Then there are patients in whom adequate medical treatment has failed; in these gastro-enterostomy, and perhaps even more so partial gastrectomy, may yield excellent results. But it is true that at medical clinics post-operative ulcer patients, who appear to have escaped surgical statistical surveys, lurk about in no small number.

During the past five years, I have been impressed by certain aspects of medical treatment. Satisfactory healing is unusual if the patient is ambulant. Complete bed rest for a minimum period of six weeks, followed by a further six weeks of quiet convalescence, is essential. In this disease the early disappearance of the pain, together with a host of economic and domestic difficulties, are, I am sure, important factors in the generally unsatisfactory results. Mental relaxation is undoubtedly as important as physical, and I have come to regard the administration of phenobarbitone as of more importance than alkalis. Alkalis are only demanded when treatment is inadequate. Under such conditions the patient demands alkalis because they relieve discomfort temporarily; but to think that they form a lining in the stomach and duodenum and maintain a low acid content is foolish. The frequency of the feeds is probably of more importance than their nature, and it is common that an adequate intake of carbohydrate, iron and ascorbic acid is sometimes overlooked in an unjustified conception of "bland". In hospital practice the results of treating these patients in a special ward are striking. The necessary regime is universal and more easily and satisfactorily carried out; the total exclusion of unsuitable foods, tobacco, and perhaps even the surgeon, makes the burden easier and recovery more rapid. The good psychological reaction under such conditions is worthy of note.

Finally, it seems to me clear that in view of the unsatisfactory state of our present knowledge, each patient must be managed according to his merits—consideration not only of the ulcer but of the patient's individual characteristics, economic factors, occupation and so on all demanding particular attention. I find it a good practice in all but the clearest cases to co-operate with a surgeon from the outset, whether surgery is immediately in question or not. If then the need for surgery arises, the importance of the state of the lungs, the presence of anæmia, and possible dietetic deficiencies cannot be over-emphasized. The risk of chest complications—all too common after gastric operations—is to be minimized by pre-operative instruction in breathing exercises and the avoidance of the too tight abdominal binder, rather than by the choice of anæsthetic. The moment for most of these considerations is before and not after operation. The difficulties of both patient and doctor are increased a hundredfold if ulceration persists or recurs after operation, and only too often it is at this stage that the physician's aid may be sought.

Section of Physical Medicine

President—L. DANYERS BAILEY, C.B.

[October 11, 1944]

Training in Physical Medicine—Looking Ahead

PRESIDENT'S ADDRESS

By L. DANYERS BAILEY, C.B.

Abstract (Full Paper appeared in *Brit. J. phys. Med.*, 1944, N.S. 7, 162)

THE President discussed the future training of medical graduates in Physical Medicine and mentioned that in July 1943 the first examination for the Diploma in Physical Medicine was held by the Examining Board of the Royal College of Physicians and the Royal College of Surgeons.

He then went on to quote Professor L. S. P. Davidson of the University of Edinburgh (see *Brit. J. phys. Med.*, 1944, N.S. 7, 98) as follows: "When an individual is placed on the roster of accredited specialists in physical medicine, this should indicate . . . that he has had the necessary education in the fundamental sciences and had devoted the requisite time to learning the practice of physiotherapy under skilled direction."

The President then alluded to the Syllabus, dealing particularly with Section 5B which lays down special training in physics and in theoretical and practical instruction in a Physical Medicine Department. He mentioned that Part I of the Syllabus dealt with Anatomy, Physiology and Physics and Part II with the diagnosis and pathology of diseases in which physical methods are employed, and the last portion included Therapeutics which was divided into preventive and remedial methods of treatment.

The President considered that the Syllabus was incomplete without the inclusion of Psychiatry and Balneotherapy. He pointed out too that the co-operation of the Chartered Society of Physiotherapy and the Association of Occupational Therapists was necessary for successful training.

He outlined a detailed programme for Postgraduate training in Physical Medicine lasting one year, which could be used as a basis for further discussion. Finally the importance of after-care of patients was stressed. At one hospital, a Re-settlement Officer, not a medical man, had been appointed. He was doing excellent work as liaison officer between possible employers and the patients, and if the scheme proved satisfactory it would be worthy of vast extension in the future.

Throughout the Address the President stressed the necessity of enthusiasm and unity among the Members of the Section without which nothing great could ever be achieved.

[November 8, 1944]

The Physical Preparation of Commandos

By Surgeon Commander G. MURRAY LEVICK, R.N.

THE conditions of modern warfare produce a demand for certain special methods in the physical training of troops as a whole but especially of Commando and Airborne Troops. For active operations the last two categories are not provided with tents and must be prepared to sleep without shelter in any weather.

More and more is this a possibility in the case of other troops also, especially in the Infantry, because battles may last for weeks, the combatants having to bivouac wherever they may happen to be and whatever the weather.

These conditions impose the necessity for a form of physical training quite distinct from the "athletic" training to which our attention has hitherto been so much devoted and when we begin to study this we find in it a scientific subject which must surely take its place as a factor in Military training.

The intention here is to explain the scientific groundwork on which we may base advice on this special aspect of training.

Men who are in the athletic sense hard and fit, may be and often are, soft in their

Eight years ago he had undertaken a gastroscopic study of those cases with persisting symptoms after gastro-enterostomy attending Sir James Walton's Follow-Up Department at the London Hospital. The outstanding observation was that all these patients had marked excess of gastric folds. Six control cases who had been cured by gastro-enterostomy showed nothing like this degree of rugosity, although the number of folds was more than in the average stomach.

These findings appeared to embody an explanation of the failure of gastro-enterostomy in some cases and its success in others: it seemed that this operation would not be followed by stomal ulceration unless the gastric mucosa was grossly redundant, probably because of habitual hyperacidity. For the last six years he had therefore gastroscoped all cases of duodenal ulcer before operation and had performed a partial gastrectomy on those with marked hyper-rugosity, and a gastro-enterostomy on the others. It was suggestive that the proportion of partial gastrectomies worked out at 25%—just about the number of failures that would have been anticipated if all the cases had been subjected to gastro-enterostomy. Of 71 duodenal ulcer patients operated upon between 1939 and 1943 he had followed up 68; 14 of these were partial gastrectomies and the rest gastro-enterostomies. The operative mortality was nil and there were only 4 cases of recurrent ulceration, one of which was due to an error of gastroscopic observation. One patient had died at the age of 70; 4 had retired from their occupations, but the other 63 were on full work, mostly as labourers, artisans and clerks. They were all on a full diet, quite unrestricted in 57 of them, though certain foods were avoided by 6 of them.

The speaker considered it too early to draw firm conclusions from these results, but he felt they justified a return to the lesser operation of gastro-enterostomy except in those cases where a gastroscopic estimation of the degree of rugosity in the stomach indicated the danger of recurrent ulceration: only then was the more hazardous operation of partial gastrectomy justified.

Section of Physical Medicine

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The intention here is to explain the scientific groundwork on which we may base advice on this special aspect of training.

Men who are in the athletic sense hard and fit, may be and often are, soft in their

resistance to exposure. It has been noticed that many of these men, who in the course of their training have been required to sleep in the open in the cold weather, have been unable to sleep and have spent the night tossing about and shivering, while a certain number have slept quite well. Obviously there has been some physiological difference between the bodies of those who could sleep and those who could not, and I shall endeavour to explain this difference as far as possible and to point out the lines on which training may be carried out so as to convert the "soft" man into a "hard" man. The importance of the subject is manifest. The fact that the soft man is uncomfortable in the cold does not so much matter. The fact that he cannot sleep matters very much indeed.

The town dweller who has lived a soft life can maintain a normal temperature only within the narrow limits of the temperature changes to which he has been accustomed because his heat centre is subnormally developed and so is the rest of his heat mechanism. Therefore it takes a long time to acclimatize such a man to bivouacking in cold weather and the reasons are easily understood.

The main sources of heat in the body are the muscles and the organs, chiefly the digestive organs, while they are actively working, but the muscles are at most times by far the largest heat producers, through their combustion of fuel food in the form of glucose in order to obtain their energy for movement; the extent of this combustion being in accordance with the demand for kinetic energy and heat.

As we lie asleep, our muscles, excepting the heart and the respiratory muscles, are motionless but still producing heat by their tone. So long as we are digesting our last meal, the heat produced by the tone of our muscles and our organs is about equal when we are lying still.

The main reason we are apt to awake cold in the early hours of the morning is because we have finished digesting our last meal and are relying chiefly on our muscular tone for our heat and this may be inadequate.

In the Antarctic when on sledging journeys in very low temperatures (a time when sensibility to such matters is at a high level) the warming effects of the morning and evening meals are particularly noticeable. Those who have to bivouac should, therefore, be specially advised to keep enough of their daily ration for a good meal at night.

Supposing now that as we sleep our temperature is falling, our heat centre may act in three ways:

(1) Muscular tone is increased throughout the body to increase combustion. The increase in heat output is thus very great because the chief weight of our bodies is in our muscles.

(2) Our blood is kept away from our radiator which is the surface of our body, by constriction of the superficial arteries.

(3) Should our temperatures still be subnormal we are made to shiver to increase output of heat by muscular work.

To explain the rationale of measures advocated in a later part of this paper, I must remind you of the reverse action of our heat centre in reducing a supranormal temperature.

(1) The superficial arteries are dilated.

(2) Muscle tone is reduced.

(3) The sweat glands are activated. Here I ask you to bear in mind the quantity of heat required for evaporation of water (i.e. 239 calories per pint), because this also has a bearing on certain advice when I discuss the bivouac later on.

This general picture of the activities of our heat centre and mechanism enables us to detect the causes of softness.

It is clear that the efficient working of the heat mechanism depends upon the bringing of a variety of structures into complete co-ordination with the brain centre as well as upon their state of nutrition, but the latter is important.

For example, the insulation of the body surface depends largely on the development of the involuntary arterial muscles. When these are weak, vasoconstriction is feeble and inefficient. Thus a soft man going out into cold air loses a lot of heat, whereas a hard man, with well-developed and practised arterial muscles, loses much less.

Confirmation of this theory is found by observing the reactions of various men to very cold weather. I have noticed that the faces of some men turn blue, while simultaneously others blanch, and that it is the well-"weathered" men who blanch while it is usually the softer who go blue, the white skin resulting from complete, the blue skin from incomplete, occlusion of the arterioles.

Bivouacking in a north-easterly wind with soaking rain may impose a much greater test of a man's heat mechanism than a much colder temperature without rain, owing to the evaporation of rain water from skin and clothing which negatives the effect of the dried-up sweat glands.

My first instruction to each batch on arrival at the training quarters was in the form of two lectures, the first devoted entirely to an explanation of the processes I have outlined.

The men were invariably attentive and interested and when their co-operation had been enlisted in this way they were very ready to carry out the measures advocated for hardening themselves against exposure for which they now understood the reasons. Without such co-operation it is quite impossible to get instructions conscientiously carried out.

Further teaching then came under two headings: (1) The training of the body to resist exposure in the open. (2) The application of science to the art of bivouacking under adverse conditions.

This last subject should be accomplished by practical instruction so that men can be shown how to secure as much comfort as possible while bivouacking under really bad conditions. For such instruction there is surely no better or tougher school than the Scottish Highlands.

To begin with, it is well to impress combatant Officers and N.C.O.s, and in Training Establishments especially, the Chief Instructors with the importance of not unduly hurrying the hardening of raw troops. It takes much longer to acclimatize the average recruit to sleeping in the open in bad weather than it takes to get him into athletic training. If you proceed too quickly you upset his health and set him back in his training. For example, if you have to train a battalion in soft condition for some operation on which they will be exposed to hardship and you have only a short time to do it in, it is useless to progress any more quickly than you would if you had ample time at your disposal. In other words, you can only reach a certain degree of hardening in a certain length of time and you must be content with that.

The next axiom is that a desirable degree of hardness for warfare can only be reached by men adapting most of their habits of life to that end. It cannot be attained by relying on certain periods of active training and spoiling that effect by interludes of softness. That is why it is so important to get the co-operation of rank and file from the word "go". The contrast between sleeping out without shelter in cold wind and rain and sleeping in a Nissen hut without heating and with doors and windows open and only one blanket, is quite appreciable. The latter would be a luxury compared with the former conditions.

But the contrast between sleeping in a hut with the doors and windows closed and perhaps a stove on in the winter and the bivouac under the usual weather conditions is far too great, and men who sleep in huts under those conditions are asking for a bad time in the "open". This should be explained to all concerned.

Moreover, just as in training for athletics if a man gets perfectly fit, runs his race and then takes little exercise for a couple of weeks, he gets out of training and has to start again, so in exposure hardening, a man may get quite hard but rapidly become soft again if he goes back to a period of comfortable conditions.

One of the chief items which I have constantly impressed on the trainees is the softening effect of our overclothing, advising that during the cold seasons they should, during their training, endeavour to wear just sufficient underclothing to keep them mostly just off the shiver with perhaps occasional slight shivering, this being just the point when they are, without over-chilling, calling upon their heat centre to increase heat production and with its mechanism to retain the heat in the body. At night they should use only just sufficient covering on their beds to enable them to sleep, which they can ascertain by experiment. If this is done intelligently, they will find that as time goes by they need less and less covering, thus approaching the desired immunity to exposure.

It is interesting to realize the extent to which the human heat mechanism can be developed by the stimulus of a perfectly natural mode of life.

Darwin, in his book "The Voyage of the Beagle" states that this ship with Darwin on board, anchored one day in the winter off the Coast of Terra del Fuego. This country, in the sub-Antarctic regions, has a cold winter and Darwin tells us that the natives came off in canoes stark naked in the freezing air, with the sleet heating on their skins, showing no signs of feeling cold. From birth, these people, probably the hardest the world has ever produced, had never worn clothes and showed the extent of hardening which such natural development of the heat centre and mechanism can produce in the human body.

Nowadays the Terra del Fuegians are softer and degenerating because they are adopting civilized ideas of life and clothing. Nothing but lifelong exposure can produce such an effect, but I think Lawrence of Arabia was a fair example of what can be accomplished in our civilization by a man who sets his mind to it at an early age. No one who has read the "Seven Pillars of Wisdom" with any understanding, can fail to realize the extent to which Lawrence had succeeded in hardening his body, not only against fatigue but hardness and had done this all his life. He tells us that in boyhood he began to cultivate

We can now see that our first step in training should be to secure by gradual stages a "stiffening up" of the barrack or camp hygiene, the later stages to be concurrent with the first experience of bivouacking. With the exception of really warm weather, this latter experience should not be begun when the men are much fatigued. A march of two or three miles to a selected spot is therefore enough. The time when the test becomes really serious is in cold and wet winter weather, and in wartime this training must go on throughout the year so it may be of the utmost importance to give instruction in the art of bivouacking under these conditions before they set out for the first exercise. A good plan is to take the men out to some selected ground, first demonstrating a suitable method by actually constructing the bivouac, then setting the men to make others for themselves.

Very often, when out on a "scheme" in the West Highlands everyone was wet by night-fall and the boots and socks certainly soaking wet. It is advisable above all other measures to impress the importance of keeping religiously a special pair of dry socks for sleeping in, and, on turning out in the morning, to take them off (whatever the temptation to keep them on) and to place them inside the battledress blouses to dry off during the day. It is difficult to get to sleep in cold weather with wet socks in wet boots owing to the amount of heat conducted from the feet through the wet socks and wet boots for the evaporation going on from the surface of the boots. The chilling of the feet is then such as to keep one awake and on wartime training men must sleep in their boots in bivouac for very good reasons. But with dry socks in wet boots the feet keep surprisingly warm. For one thing, the leather does not hold much water and it may be long before the inside of the socks become damp and by that time we are asleep. There may be another explanation: Sir Leonard Hill pointed out that if you put on a dry cotton vest for some considerable time it actually warms up through heat given off by the condensation in the cotton of water vapour evaporating from the body, the latent heat of the water vapour being thus liberated. The same thing may happen in the dry socks in wet boots.

There is a portion of the body from which heat escapes perpetually and copiously even when conditions call urgently for its retention. If this is not carefully explained to the men they may not realize the importance of guarding against it when becoming chilled in bivouac. Every breath of cold air inhaled is heated by conduction in the lungs to close on body temperature and, through evaporation, quite saturated with water vapour. The consequent loss of heat is very great (especially from the evaporation), and completely lost from the body at each expiration. The heat centre has no control here. Without this explanation, men do not realize how much of this loss can be prevented by merely covering the mouth with a woollen scarf, corner of the blanket or any other woollen fabric. Thus, much of the heat is left behind on expiration in the fabric which is also moistened by condensation of the water vapour. In consequence, the air inspired through the fabric is partially warmed and with relative humidity raised enough appreciably to reduce the pulmonary evaporation.

Some care was needed to prevent many of the young Commandos from letting their enthusiasm for getting hard carry them too far. The promulgation of the necessary knowledge among the training staffs is not a difficult matter, and having recently been for that purpose on a lengthy tour of training establishments I found everywhere a surprising keenness among the personnel to learn all about it. One of the most important things to learn by experience is how far the hardening process can be carried with advantage to the trainee. For instance, if certain troops were being trained for a particular operation on which they had to stand for an hour up to their waists in cold water, one would not go as far as that in the course of their training because it would do them harm instead of good. The fact that training must always keep within physiological limits must never be overlooked. The actual details of the training depend very much on local conditions. The main idea must be by gradual stages to provoke and strengthen the reaction of the entire heat mechanism.

This form of training is concurrent with other subjects and it may be that schemes lasting several days over such country as the Western Highlands, with the shelter of trees hard to find, have to be carried out by troops whose hardening has not yet gone very far. Here one can only, as far as possible, temper the wind for lambs not shorn but in denim battledress and with only one blanket.

To endure successfully severe exposure in the field, a man must be able to fend for himself and learn ingenuity in devising methods to meet contingencies as they arise. This he cannot do without simple scientific instruction. The subject is one which cannot fail to interest the medical branches of the combatant Services and by keeping to the essential and easily understood factors I have outlined, thus talking to, but not down to, the rank and file, they can impart to them much valuable information.

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[November 28, 1944]

DISCUSSION ON THE INFLUENCE OF NUTRITIONAL FACTORS IN "LIVER DISEASE"

Professor H. P. Himsworth: Recently, as the result of investigations into the effects of abnormal diets, light has been thrown upon problems in the causation of various liver diseases. That diet influences liver injury is no new discovery. As long ago as 1914 Opie and Alford showed that the susceptibility of dogs to chloroform poisoning was largely influenced by the character of the diet they were receiving. But this work, and the line of research that grew out of it, is concerned simply with the effect of diet in exaggerating or mitigating damage resulting from exposure to definite hepatic poisons. The first demonstration that dietary factors alone can initiate liver injury was given by Weichselbaum in 1935. He noted that a diet, generally deficient in protein and particularly deficient in sulphur amino-acids, caused death with "hæmorrhage" into the liver. At the time this work largely escaped attention and it was not until 1939 and 1940, when claims were made to have produced cirrhosis of the liver by dietetic means, that the importance of diet in the production of liver disease was realized (Gyorgi and Goldblatt, 1939; Rich and Hamilton, 1940). Further papers making similar claims rapidly followed and in some of them it was noted that, infrequently and inconstantly, some of the animals taking diets designed to produce cirrhosis died, or became ill before developing that lesion, with "hæmorrhages" or necrosis of the liver (Gyorgi and Goldblatt, 1939; Webster, 1941). In this latter group the animals who survived the necrosis showed in animals on certain deficient diets, agreement was, therefore, soon reached. But in another, that of causation, differing results were obtained, and it is hardly an exaggeration to say that practically every dietary factor, save carbohydrate, has at one time or another been credited with a rôle in the production of liver injury. Glynn and I believe that this confusion arises largely from a failure to recognize that lesions in the liver are of two kinds (Himsworth and Glynn, 1944b). One is a massive acute necrosis which either kills or leads to post-necrotic scarring and nodular hyperplasia; the other is a diffuse hepatic fibrosis, of insidious development, which closely resembles portal cirrhosis. Both, in their final stages, produce a fibrotic lesion of the liver, and it is this finding which has led to their being confused together under the single term of "dietary cirrhosis of the liver". As a consequence the necrosis, occasionally observed in the livers of animals on certain diets, has been regarded by most workers as but a transient stage in a single sequence which leads to portal cirrhosis (Gyorgi and Goldblatt, 1942). If, as we believe, the two lesions are distinct, and different dietary factors enter into the production of each, then attempts to refer both to a single dietary influence might be expected to lead to confusing results and conflicting opinions.

EXPERIMENTAL DIETETIC INJURY OF THE LIVER IN RATS

(a) *Massive hepatic necrosis (acute yellow, or subacute red, atrophy) with its sequelæ.* postnecrotic scarring and nodular hyperplasia.—By appropriate modifications of diet it has been shown that the development of this lesion is dependent upon the amount of particular protein consumed (Himsworth and Glynn, 1944b). When this falls below a certain level massive hepatic necrosis develops. Neither the vitamin, choline, fat, nor carbohydrate content of the diet influences this result. The sole factor is the amount of

protein consumed. But different proteins vary in their ability to prevent the lesion. Casein for example is effective in small amounts, yeast protein, when the sole source of protein, is ineffective even in large amounts. The most obvious difference between these two proteins is that the former is rich, and the latter poor, in the amino-acid methionine, and it has been found that yeast protein can be made to protect as effectively as casein when it is enriched by the addition of adequate amounts of methionine (Himsworth and Glynn, 1944c).

When rats are given a diet appropriately low in protein they remain apparently well for weeks. Then suddenly they fall ill. Some die in a matter of hours and show massive necrosis of the liver; others survive in precarious health to develop jaundice, ascites and oedema, and at death these show nodular hyperplasia. There are several points in this sequence which merit attention. First, that before the illness develops there is a long latent period and during the whole of this the animal is exposed to the defective diet; second, that the illness is of sudden development and that until its onset the liver is normal in appearance; third, that complete recovery does not occur and that, in those animals which survive, scarring of the liver is always found.

Of particular interest is a variant of this lesion—partial, massive, hepatic necrosis. In this condition the necrotic processes, and their sequelae, are limited to the left lobes of the liver. This lesion develops in animals receiving sufficient protein to prevent the development of generalized massive necrosis but insufficient to protect entirely. Injection of Indian ink into the spleens of normal animals shows that the ink is carried to those parts of the liver in which the partial lesion develops (Glynn and Himsworth, 1944; Himsworth and Glynn, 1944b). Now it has been shown in several species that the blood from the superior mesenteric vein does not mix freely with that from the splenic vein in its short transit through the portal vein. As a result the former goes mainly up the right branch of the portal vein to the right lobes of the liver; the latter up the left branch to the left lobes. As the products of protein digestion from the small intestine are carried in the blood of the superior mesenteric vein it is evident that, when the diet is deficient in protein, this deficiency will be more advanced in the left lobes. The occurrence of partial massive necrosis is to be explained on these lines. The importance of the partial lesion is that it indicates that circulatory factors may determine whether or not a dietary necrosis shall develop.

(b) *Diffuse hepatic fibrosis of the liver (portal cirrhosis).*—The common feature of diets which cause this lesion is that they all produce, and maintain, heavy fatty infiltration of the liver (Himsworth and Glynn, 1944b). To do this the diets may be either rich in fat or deficient in lipotropic factors.

The clinical course, and the pathological changes in the liver, of rats on such diets are in marked contrast to those in rats developing massive acute necrosis. First, diffuse hepatic fibrosis requires months rather than weeks for its development. Second, there are no episodes of acute illness; for several months the animals remain well and then their health gradually deteriorates. Third, the pathological changes in the liver develop gradually, not fulminantly as in acute necrosis. Fourth, there is no evident necrosis at any stage. Fifth, heavy fatty infiltration of the liver is an essential precursor and concomitant of diffuse fibrosis, while the development of acute necrosis is independent of such infiltration. These points are sufficient to indicate that, at least on first analysis, diffuse hepatic fibrosis and massive acute necrosis are distinct conditions. But it is still possible that fundamentally they are related and that their manifest differences are due to local conditions inside the liver. Hepatic necrosis occurs when the parenchymal cells receive insufficient supplies of a factor contained in protein. This may occur either because the blood contains too little or, when sufficient is present, because of an inadequate blood flow through the liver. It is easy to imagine that when the liver cells are choked with fat the flow through tortuous, intralobular sinusoids may be so retarded that by the time the blood reaches the central cells it is largely depleted of nutriment. Under such circumstances unobtrusive death of the centrilobular cells may occur continually; and, as Cameron and Karunaratne (1936) have shown, repeated attacks of centrilobular necrosis lead eventually to portal cirrhosis. In this connexion certain experiments, on the result of intravenous injection of methyl-celluloses, are of interest (Hueper, 1944). These inert substances accumulate in such quantities in the Kupffer cells of the liver as to distend the whole organ. After several weeks centrilobular necrosis develops even though the animals are taking a normal diet. Connor (1937) has put forward a very similar suggestion to explain portal cirrhosis in man and in diabetic dogs with fatty livers. He considers that fatty infiltration of the parenchymal cells so

interferes with intralobular circulation of blood that the central cells are damaged by anoxia.

Whatever the ultimate decision on this point, however, experimental massive hepatic and diffuse hepatic fibrosis are sufficiently distinct, clinically and pathologically to require that, at least in the present state of knowledge, they be considered separately in relation to hepatic disease in man.

MASSIVE HEPATIC NECROSIS IN MAN

In certain parts of the tropics a massive hepatic necrosis occurs which, the evidence suggests, may develop as the direct result of a dietary deficiency of protein. In Uganda this lesion and its sequel, nodular hyperplasia, are relatively common among the native population (Muwazi and Trowell, 1942). The native diet is one of the most deficient in protein found in the world. A so-called cirrhosis of the liver is common amongst Africans on the Rand. Gillman (1944a) found that on giving their diet to rats a nodular hyperplasia confined to the left lobes of the liver developed. Such a partial lesion is, in our experience, diagnostic of a previously occurring partial massive necrosis, for true portal cirrhosis (diffuse hepatic fibrosis) is widespread throughout the organ in all its stages. A fibrosis of the liver is also common in certain parts of India and Hughes and Shrivastava (1927) have correlated this with a preceding severe attack of jaundice. Such jaundice is particularly apt to occur after a severe epidemic of malaria has incapacitated a community, and fatal cases, although they show no evidence of active malaria, have massive hepatic necrosis. From time to time in various parts of the tropics reports are received of an outbreak of "yellow fever". On investigation no yellow fever is found but the livers from fatal cases show massive necrosis. By the courtesy of Dr. Hugh Smith of the Rockefeller Foundation we have been able to examine sections from such cases obtained from an area in South America. They were microscopically indistinguishable from those of rats with dietetic massive necrosis. It is noteworthy that such outbreaks seem only to occur among people living on diets grossly deficient in protein.

The massive hepatic necrosis occurring in temperate climates presents a different problem (Himsworth and Glynn, 1944a). Here there is no indication of a direct dietary deficiency of protein. The massive necrosis seems to occur as a complication of some other condition. These conditions fall into two groups: first, those which do not usually give rise to liver damage; second, those which characteristically give rise to mild liver damage from which recovery is the rule. Pregnancy and exposure to such poisons as T.N.T. and cinchophen are examples of the first group. It has long been known that massive necrosis, although a rare condition, is particularly prone to attack pregnant women. It is also evident that during pregnancy the nutritional requirements of the foetus are satisfied at all costs, even at the expense of the mother. If because of a poor diet, anorexia or persistent vomiting, the mother is relatively starved, conditions are ripe for the development of nutritional deficiency. The suggested mechanism of the massive necrosis seen in some T.N.T. workers is best explained by considering the investigations on selenium poisoning. Rats fed on grain grown on soil rich in selenium develop an hepatic necrosis and nodular hyperplasia apparently identical with that seen in rats on a low protein diet. This selenium necrosis is prevented by the addition of casein or methionine to the diet. In the protein of plants grown on soil rich in selenium it is found that this element has replaced the sulphur in the methionine and apparently such selenium-amino-acids are inutilizable. T.N.T. combines with amino-acids. It is suggested that this combination is inutilizable. These are examples of what may be called conditioned amino-acid deficiencies.

But the majority of cases of massive hepatic necrosis develop as complications of conditions such as infective hepatitis, yellow fever vaccine jaundice, chloroform and phosphorus poisoning, which habitually cause liver damage. The liver damage normally found in these conditions is, however, quite different. They cause a zonal, not a massive, necrosis, and from this complete recovery usually, if not always, occurs. We have, therefore, to explain why massive necrosis tends to supervene on a zonal necrosis. Livers which are the seat of widespread zonal necrosis are tense and swollen. It is suggested that the tension inside the liver capsule impedes the circulation. If now the blood is poor in protein nutrients the slowly percolating blood supplies insufficient nutriment to the cells and massive necrosis occurs; if, however, it is rich in such nutrients the majority of the cells can survive and later by multiplication restore the damaged organ so that the patient recovers. The outcome thus depends upon the balance struck between the amount of protein nutriment in the blood and the retardation of intralobular circulation consequent upon the swelling of the parenchymal cells. In this connexion it is of interest that

pregnant women who contract infective hepatitis are more prone than males and non-pregnant women to die from massive hepatic necrosis (Cockayne, 1912); and that in recent studies of yellow fever vaccine hepatitis the mortality rate from massive hepatic necrosis among well-fed American troops was 0.2% (Findlay *et al.*, 1944) while among ill-fed Brazilian natives it was 2.4% (Fox *et al.*, 1942).

Whilst in no single instance cited above is it proven that the observed massive hepatic necrosis or nodular hyperplasia, results from protein deficiency the indications from all point in the same direction. The hypothesis that massive hepatic necrosis in man may result from an inadequate supply of protein to the liver, whether this inadequacy is brought about directly or indirectly, must therefore be considered as a serious possibility.

HUMAN PORTAL CIRRHOSIS

In Western countries portal cirrhosis is traditionally associated with alcoholism. All recent investigations have shown, however, that alcoholism cannot be its essential cause, and is, at most, a contributory factor (Jolliffe and Jellinek, 1941). In Africa and the East strong evidence against such an association has long been available for there classical portal cirrhosis is widespread amongst native peoples who, either by religion or poverty, are prevented from alcoholic excess. Recent experimental work suggests an explanation of these observations.

The essential pre-requisite in the production of experimental portal cirrhosis is apparently a heavy, prolonged, fatty infiltration of the liver, whether this is produced by high-fat diets or by low-fat diets deficient in lipotropic factors. In the early stages of alcoholism such a fatty infiltration is common; in the later stages the common lesion is portal cirrhosis. So impressed were the French clinicians of the nineteenth century with this sequence that they distinguished an early stage of "steatosis" of the liver, when the organ was enlarged, from a later stage of cirrhosis of the liver, when the organ was shrunken and atrophic (Trousseau, 1870). Consideration of the nutritional aspects of alcoholism suggests how such a preceding fatty infiltration could be brought about, and maintained. Alcohol contains no lipotropic factors. In excess it produces gastritis, impairs appetite and so limits the addict's intake of food. Further, alcohol is expensive, and so are the foods rich in lipotropic factors such as protein. All these factors tend in the same direction, to the production of a fatty liver. The evidence from Africa and the East points to a similar explanation for the portal cirrhosis which is so common in certain tropical regions. There a condition characterized by heavy, fatty infiltration of the liver is known to occur amongst native peoples living on poor diets. By the courtesy of Dr. H. C. Trowell of Kampala, Uganda, I have been able to examine sections from such a case and these show such a distension of the liver cells with fat as, in experimental animals, would presage the development of portal cirrhosis. Recently Dr. Joseph Gillman (1944b) of the Witwatersrand University has informed me that, using the aspiration biopsy technique, he has obtained from the same patients successive samples of liver showing every stage from such a fatty infiltration to classical portal cirrhosis. The diets eaten by the natives, both in Uganda and on the Rand, are low in protein and deficient in those vitamins which in nature are associated with strong lipotropic factors such as choline.

It thus appears that all over the world portal cirrhosis is associated with the consumption of defective diets which are productive of fatty infiltration of the liver; and, further, that such fatty infiltration of the liver may develop into portal cirrhosis. Whether alcohol in excess may contribute to the development of this lesion by a direct toxic action on the liver cells is still unsettled. But even if it can, it appears that such a contribution is gratuitous and that the apparent association of portal cirrhosis with alcohol can more easily be explained as a result of the malnutrition consequent upon alcoholism.

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Dr. L. E. Glynn: There are two aspects of the subject of nutritional liver injury which Professor Himsworth has intentionally omitted. The first is the distinction between the two types of liver lesion produced by dietary means in experimental animals. The second is a comparison of these lesions with their counterparts in the human.

Livers that have undergone almost complete necrosis are swollen, friable, and pale yellow in colour, with fine haemorrhages present both on the surface and in the depths of the organ. Where only part of a lobe is involved the individual lesions are very sharply defined with the gross appearance of infarcts, but vascular thromboses are extremely rare and when present are secondary to the necroses. Slightly older lesions such as those seen in the animals dying in the seventh week show evidence of shrinkage; where an entire lobe is affected this is obviously reduced in size relative to the liver as a whole; where only part of a lobe is affected this is depressed below the general surface of the unaffected portion. These shrunken and depressed areas are dark red in colour either uniformly or studded with raised yellow nodules (fig. 1).

Animals surviving beyond the seventh week show the oldest lesions, almost invariably in the left half of the liver with or without more recent lesions elsewhere. The former exhibit considerable shrinkage and distortion frequently accompanied by surface nodularity (fig. 2). The consistency is firm, not friable, and the colour a characteristic yellow-brown with reddish-brown reticulate markings.

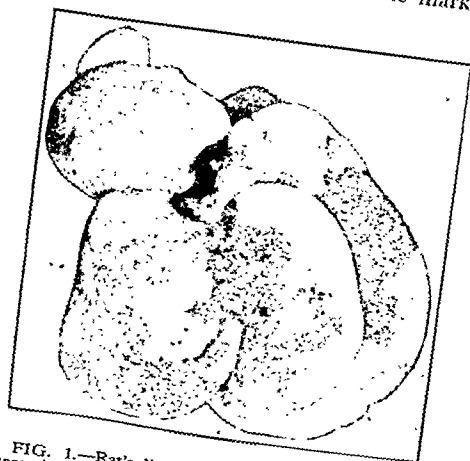


FIG. 1.—Rat's liver in generalized massive acute necrosis, showing depressed red areas in the left half where the lesions are oldest, lesions three to fourteen days old.
 × 4.3.

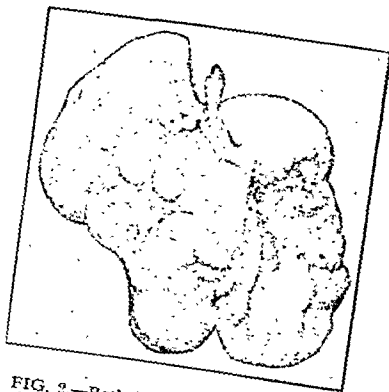


FIG. 2.—Rat's liver shrunken and distorted as the result of scarring and nodular hyperplasia following massive acute necrosis. Left half of middle lobe has been removed to expose the deeply-scarred left lobe. Lesion probably two months old.
 × 7/6.

From the above description it is apparent that macroscopically the lesions correspond in remarkable detail with those of acute yellow atrophy in man. Microscopically the correspondence is equally striking. The necroses are usually massive, i.e. involve the whole of several adjacent lobules but where zonal are centrilobular or periportal with about equal frequency. In the areas of massive necrosis small clusters of surviving liver cells may be seen often in close proximity to a portal canal, but frequently distributed haphazardly. The structures in the portal tracts and the Kupffer cells also survive even in areas of extensive necrosis, but the sinusoids appear empty owing to compression by the swollen liver cells.

The depressed red areas of the next stage result from the re-absorption of the necrotic cells associated with dilatation of the previously collapsed sinusoids. This results in some

pregnant women who contract infective hepatitis are more prone than males and non-pregnant women to die from massive hepatic necrosis (Cockayne, 1912); and that in recent studies of yellow fever vaccine hepatitis the mortality rate from massive hepatic necrosis among well-fed American troops was 0.2% (Findlay *et al.*, 1944) while among ill-fed Brazilian natives it was 2.4% (Fox *et al.*, 1942).

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trast with the livers of methionine-deficient animals, actual necrosis of liver cells is rarely seen. At most some slight centrilobular necrosis may be noted.

Nutritional deficiency in the experimental animal may, therefore, lead to two types of scarred or cirrhotic liver. The first is the end-result of an acute massive necrosis, or yellow atrophy, the second a uniform diffuse fibrosis or portal cirrhosis. They differ in

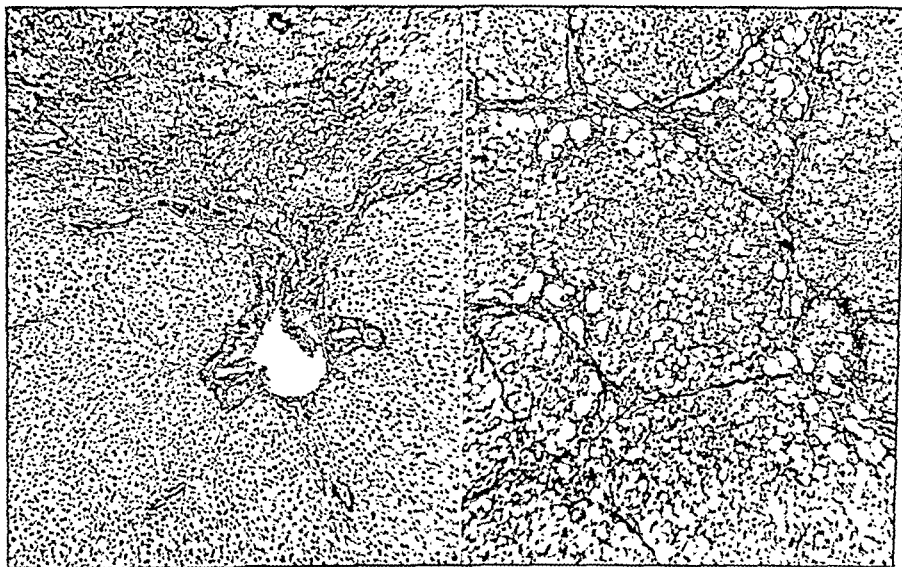


FIG. 4.—Section through a coarse post-necrotic scar. The scar extends across the upper edge of the field: below the liver pattern is normal showing that the fibrosis is not diffusely distributed. Laidlaw's reticulin stain. $\times 50$.

FIG. 5.—Diffuse hepatic fibrosis. Section shows invasion of the liver lobules by the increased connective tissue radiating from the portal tracts, with resulting obliteration of the normal lobular pattern. Laidlaw's reticulin stain. $\times 50$.

(Fig. 1 is reproduced by kind permission of the Editor of the *Journal of Pathology and Bacteriology*; figs. 3 and 5 by kind permission of the Editor of *Clinical Science*.)

ætiology and evolution and they may be distinguished by the criteria of postnecrotic nodular hyperplasia laid down by Mallory in 1911, namely gross irregularity in the distribution of the lesions, presence of areas of recent necrosis and evidence of compensatory hyperplasia of intact liver lobules in uninjured parts of the liver. To these may be added the greater severity of involvement of the left half of the liver, and the presence of hæmosiderin-laden macrophages in the scar tissue.

Reference.—MALLORY, F. B. (1911) *Bull. Johns Hopkins Hosp.*, 22, 69.

Professor John Beattie discussed the possibility of dietetic factors influencing the susceptibility of a population to epidemic forms of hepatitis. He pointed out in this connection that variations in the virulence of the infective agent and the degree of immunity of the population must also be taken into consideration when investigating any isolated epidemic. Because of the presence of at least three possible variables, investigation of small local epidemics cannot be expected to produce other than equivocal results. The possibility that some relation between protein intake and incidence of hepatic damage may exist cannot however be excluded. In two populations on different levels of protein intake the incidence of infective hepatitis during a two-year period was markedly higher in the population on the lower intake. Investigation of individual cases of infective hepatitis demonstrated clear evidence of low protein intake in some but not in others. Supplementation of the diet with methionine was apparently effective in protecting patients receiving arsenical treatment for syphilis against hepatic damage.

If a methionine deficiency were the factor determining the susceptibility of an individual to the virus agents causing infective hepatitis and post-arsphenamine jaundice, one would expect that administration of methionine to a patient suffering from one or other of these

instances in sinusoidal rupture and hæmorrhage but rarely to a conspicuous extent. The portal tracts become infiltrated with cells, mostly polymorphonuclear leucocytes, whilst the central zones become crowded with mononuclear cells mainly of histiocytic type presumably derived from the Kupffer cells. The density with which these mononuclear cells accumulate leads to apparent compression and re-collapse of many of the sinusoids, the necrotic area being eventually replaced by an extremely cellular, poorly vascular granulation tissue. This is next invaded by proliferating bile ducts from the portal tracts which may be slight or very pronounced. The cellular infiltration of the portal tracts which at first is slight and mainly polymorphonuclear is more marked at this stage and mainly histiocytic. Portal tracts in the vicinity, but not included in the area of necrosis, frequently, but not invariably, show a similar infiltration.

The replacement of the necrotic tissue by a cellular granulation tissue results in considerable reduction in volume which becomes further accentuated by the usual maturation changes of such tissue, namely, reduction in cellularity accompanied by formation of connective tissue fibres. The latter are almost exclusively of the argentophil reticulum type (fig. 4); very few collagen fibres stainable by van Gieson's mixture are seen. But even in the oldest lesions the tissue is still rich in cells the majority of which retain their histiocytic appearance. In most instances these cells are obviously pigmented, brown pigment occurring in fine dust-like granules. Some but not all of this pigment gives a positive Prussian blue reaction for iron.

Regenerative activity by the surviving liver cells becomes apparent at about the same time as the proliferation of the bile ducts. This is most marked in the vicinity of the portal tracts and rare in the more isolated groups of liver cells in which signs of necrobiosis may now frequently be seen. In those lobes where necrosis of the liver cells has been complete the area comes to consist entirely of pigmented cellular scar tissue. Where groups of liver cells survive and regenerate a form of hepatic cirrhosis results in which nodules of liver cells are present, irregular in internal arrangement and separated by wide bands of cellular scar tissue, a picture indistinguishable from so-called nodular hyperplasia in the human liver following subacute yellow atrophy. As in the human the lobes least affected in the acute stage may show remarkable compensatory hyperplasia in the healed stage.

The second type of liver lesion producible in rats by appropriate diet is a diffuse fibrosis comparable to human portal cirrhosis. The essential feature of this cirrhogenic diet is a deficiency in lipotropic factors resulting in severe accumulation of fat in the liver cells.

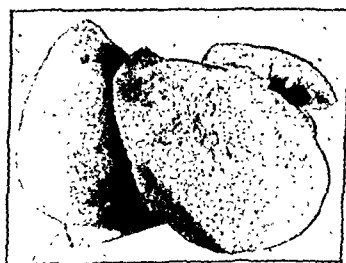


FIG. 3.—Diffuse hepatic fibrosis; "portal cirrhosis". The whole surface of the organ is finely granular as a result of a diffuse fibrosis. There are no deep scars such as occur in postnecrotic scarring. $\times 5/4$.

For the first hundred to hundred and fifty days on the diet the only demonstrable hepatic abnormality is severe fatty infiltration with distended liver cells and apparent sinusoidal compression. From about this time onwards a progressive fine uniform granularity appears (fig. 3) associated with increase in the fibrous tissue of the portal tracts and to a lesser extent round the centrilobular veins. With extension of the fibrous tissue from portal tract to portal tract, an accentuation of the normal lobular pattern may result. The fibrosis, however, does not remain confined to these areas, but soon invades the individual liver lobules ensnaring groups of liver cells in the process and completely obliterating the normal lobular pattern (fig. 5). Regenerative hyperplasia in the ensnared groups of cells results in further distortion of this pattern. A variable degree of bile-duct proliferation completes the resemblance to human portal cirrhosis. In sharp con-

Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[November 3, 1944]

Spinal Analgesia in the Very Young and Further Observations.

By W. ETHERINGTON-WILSON, F.R.C.S.

TEN years ago I read a paper and showed a long film in connexion with the anatomical, physical and experimental side of spinal analgesia (*Proc. Roy. Soc. Med.*, 1934, 27, 323). The work suggested a choice of technique including the method of timing a light solution travelling up the vertical spinal canal, in order to obtain the required levels of block: the essence of control.

I now have the careful record of 1,600 supervised cases. The alterations in technique have been few and minor. I have now a simple formula, for more accurate estimation of the timing in seconds. It has also been used for spinal analgesia in a small series of babies and the very young.

Vertical ascent.—The advantages of the upward travel of a hypobaric solution along the straight, or almost straight, spinal chimney, bear repetition. (1) Automatic and thorough mixing in the shortest possible time. (2) Once mixed the solution is very rapidly fixed and no alteration in segment level can be obtained. (3) Ascent is slow, as the fluid ploughs its way up through the denser cerebrospinal fluid and past other solid obstructions: this braking action is not fully appreciated. (4) The Trendelenburg position immediately stops ascent: if the rate of travel is known, segmental levels can be obtained. The spinal analgesic is therefore fully controlled. (5) It is not a volumetric method. It allows of the smallest possible effective dosage. (6) Any powerful solution being used is diffused over a long length of canal, well mixed and therefore not liable to inflame nervous tissue.

Formula.—Owing to the varying lengths of patients' backs irrespective of stature, it soon became obvious that the length of the high spinal run should be measured, i.e. 4th thoracic spine to thumb-nail impression in the 4th lumbar space, with the patient in the vertical, inclined, lumbar-puncture position, on the operating table. For all light nupercaine solutions the formula figure is 5. For spinocaine the figure is 2. Suppose the high spinal run is 16 in.: 16 by 2, or 32 seconds using spinocaine. For all block using nupercaine, and 16 by 5, or 80 seconds, it happens that a low spinal (L.1, D.12) Worked out anatomically and from experience, it happens that a low spinal (L.1, D.12) is one-half of the high or 40 seconds, and a medium spinal (9-10 D.) is $\frac{3}{4}$ of the high or 60 seconds, with certain particular dosage. Timing commences as soon as the piston is pressed and the injection of nupercaine must be completed within 15 seconds. Interval blocks between high, mid and low can be obtained. The lumbar puncture needle is only removed at the last moment, the thumb being kept on the piston throughout the operation; the patient is now sat bolt upright.

I have previously pointed out that the bigger the injection, the more rapid the rise. In order to simplify matters, I have for years recommended to the beginner and indeed to the experienced, a uniform dosage of 13 to 14 c.c. of nupercaine or $1\frac{1}{2}$ to 2 c.c. of spinocaine for all heights. In this formula, therefore, there is only to be remembered, the fixed dosage, the formula figure of 5 or 2 when using nupercaine (S.G. 1.003) or alcoholic spinocaine (S.G. less than 1): also the fact that low and mid-spinals are half

diseases would result in rapid improvement. In mild cases it is difficult to prove that such an improvement occurs as a result of the methionine but in the more severe types rapid improvement is clearly the result of the methionine medication. In the latter type of case methionine was given in large doses by vein with good results. It was emphasized that intravenous methionine infusions are not free from danger and precautions must be taken to guard against ketosis and acidosis following such treatment.

Professor Beattie stressed the importance of ensuring an adequate protein intake during convalescence. This is of particular importance when experiments are designed to test statistically the effect of methionine in promoting the cure of the common and mild type of infective hepatitis.

Major Clifford Wilson said that there was no convincing evidence that dietary deficiency was a factor in determining the course of infective hepatitis in this country. He had conducted therapeutic trials with methionine on 100 men, alternate cases serving as controls. 5 g. of methionine were given daily by mouth. There was no significant difference in the treated and control groups in either clinical or biochemical criteria of severity. It was concluded that addition of methionine in amounts equivalent to doubling the protein intake had no demonstrable effect on the disease.

Professor Himsworth, in replying to questions, stressed two points. First that his results did not prove that massive hepatic necrosis was directly due to methionine deficiency. To prove this experiments in which amino-acids provided the only source of dietary nitrogen were needed. What had been shown was that this lesion was produced by a low protein diet, particularly one deficient in sulphur amino-acids and prevented by methionine. Second, he said that the results gave no indication that the incidence of hepatitis due to poisons or viruses could be influenced by diet. They did, however, suggest that a high protein diet, or methionine, might prevent such cases developing the complication, massive hepatic necrosis.

Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[November 3, 1944]

Spinal Analgesia in the Very Young and Further Observations.

By W. ETHERINGTON-WILSON, F.R.C.S.

TEN years ago I read a paper and showed a long film in connexion with the anatomical, physical and experimental side of spinal analgesia (*Proc. Roy. Soc. Med.*, 1934, 27, 323). The work suggested a choice of technique including the method of timing a light solution travelling up the vertical spinal canal, in order to obtain the required levels of block: the essence of control.

I now have the careful record of 1,600 supervised cases. The alterations in technique have been few and minor. I have now a simple formula, for more accurate estimation of the timing in seconds. It has also been used for spinal analgesia in a small series of babies and the very young.

Vertical ascent.—The advantages of the upward travel of a hypobaric solution along the straight, or almost straight, spinal chimney, bear repetition. (1) Automatic and thorough mixing in the shortest possible time. (2) Once mixed the solution is very rapidly fixed and no alteration in segment level can be obtained. (3) Ascent is slow, as the fluid ploughs its way up through the denser cerebrospinal fluid and past other *solid* obstructions: this braking action is not fully appreciated. (4) The Trendelenburg position immediately stops ascent: if the rate of travel is known, segmental levels can be obtained. The spinal analgesic is therefore fully controlled. (5) It is not a volumetric method. It allows of the smallest possible effective dosage. (6) Any powerful solution being used is diffused over a long length of canal, well mixed and therefore not liable to inflame nervous tissue.

Formula.—Owing to the varying lengths of patients' backs irrespective of stature, it soon became obvious that the length of the high spinal run should be measured, i.e. 4th thoracic spine to thumb-nail impression in the 4th lumbar space, with the patient in the vertical, inclined, lumbar-puncture position, on the operating table. For all light nupercaine solutions the formula figure is 5. For spinocaine the figure is 2. Suppose the high spinal run is 16 in.; 16 by 5, or 80 seconds, is the timing for a high block using nupercaine, and 16 by 2, or 32 seconds using spinocaine.

Worked out anatomically and from experience, it happens that a low spinal (L.1, D.12) is one-half of the high or 40 seconds, and a medium spinal (9-10 D.) is $\frac{3}{4}$ of the high or 60 seconds, with certain particular dosage. Timing commences as soon as the piston is pressed and the injection of nupercaine must be completed within 15 seconds. Interval blocks between high, mid and low can be obtained. The lumbar puncture needle is only removed at the last moment, the thumb being kept on the piston throughout the operation; *the patient is now sat bolt upright.*

I have previously pointed out that the bigger the injection, the more rapid the rise. In order to simplify matters, I have for years recommended to the beginner and indeed to the experienced, a uniform dosage of 13 to 14 c.c. of nupercaine or $1\frac{1}{2}$ to 2 c.c. of spinocaine for all heights. In this formula, therefore, there is only to be remembered, *the fixed dosage, the formula figure of 5 or 2 when using nupercaine (S.G. 1.003) or alcoholic spinocaine (S.G. less than 1):* also the fact that low and mid-spinals are *half*

diseases would result in rapid improvement. In mild cases it is difficult to prove that such an improvement occurs as a result of the methionine but in the more severe types rapid improvement is clearly the result of the methionine medication. In the latter type of case methionine was given in large doses by vein with good results. It was emphasized that intravenous methionine infusions are not free from danger and precautions must be taken to guard against ketosis and acidosis following such treatment.

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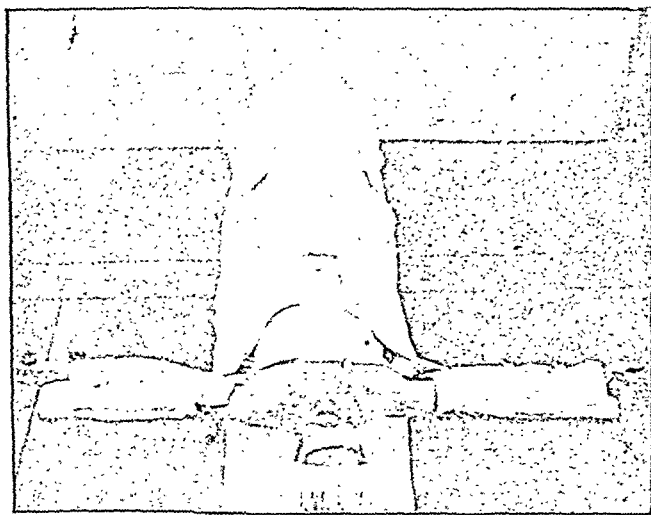
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Trendelenburg position.—High tilts are unnecessary for the co-operative surgeon. 15 degree tilts and more are steep and can be dangerous, on account of cerebral congestion, cyanosis AND WORSE; the possibility of the downward flow of heavy uncontaminated cerebrospinal fluid from the sacral canal, carrying the solution with it towards the head, must be borne in mind. I now recommend approximately an 8 degree slope which must be accurately measured. In complete intestinal obstruction where the abdomen is not particularly tympanitic, i.e. where the small intestine is loaded with heavy fluid contents, a steep slope down is particularly dangerous, because of pressure on the diaphragm and cardiac area. It is always wise to empty the stomach and keep the tube *in situ*, during the first half-hour or so after the lumbar puncture. A sloped trolley returns the patient to the tilted ward bed.

For positioning the arms when the patient is in the dorsal position, I use a flat wooden or metal board 60 in. by 5 in., hinged centrally. This support passes under the sorbo mattress, is padded at the outer thirds but not where it passes under the table mattress, for the purpose of a light fixation and abduction of the arms. The advantages of this posture are: No pressure on the chest. Easy access for examination of pulse and for intravenous therapy if necessary. Comfort (see illustration).



Shows padded cloth and tape spectacles: abducted arms lightly fixed by arm cover with three tapes, allowing easy exposure of upper arm for infusions, injections or B.P. readings. Chest excursion unhampered. A good position for all forms of anaesthesia. The table above is tilted 8 degrees head-down for spinal analgesia.

Prone position.—In a series of cases tested out I am satisfied that this posture has no place in my technique. Once a solution is mixed with the cerebrospinal fluid the prone position will not give a stronger douche to the dorsal roots. It is an unnecessary and unjustifiable manipulation of the patient.

Skin tests.—Except for an occasional demonstration, I never test the height of block before operation, apart from the information gained by the clipping of towels in position. There is time for testing after most operations; many towel clip tests are quite unreliable for the simple reason that the patient has been premedicated. Some hardly feel the prick, some feel it but cannot be bothered to respond, or may be incapable of a trustworthy localization. I have seen an anaesthetist practise passing a nasal intratracheal tube during an operation under a low spinal analgesia for hernia, with little or no objection by the patient. I have frequently got no response by pricking the scalp.

Multiple spinals.—131 cases had more than one spinal block. The figures above the line relate to the number of cases and below the line to the number of spinals.

112	10	5	2	1	1
2	3	4	5	6	8

and three-quarters of the high respectively. This formula, using nupercaine 1:2,500 or 1:2,000, is applicable to babies and children (see table) but here of course the dosage

DOSAGE AND TIMING BY FORMULA.

Multiple	Sp. Analg. in the Young.		Dose nupercaine 1:2,000
	Back to 4th th. sp.	Time in seconds high sp.	
5	3½	18	3 c.c.
5	4	20	2 c.c.
5	5	25	2½ c.c.
5	6	30	3 c.c.
5	7	35	4 c.c.
5	8	40	6 c.c.
5	9	45	7 c.c.
5	10	50	8½ c.c.
5	11	55	10 c.c.
5	12	60	11 c.c.

Above = for high spinal = 5 th. seg.;
 ½ of high = mid-spinal = 9-10 th. seg.;
 ¼ of high = low spinal = 12D., 1L. seg.

varies according to size. A formula for any hypobaric solution of known and constant specific gravity may be easily worked out.

Back measurement.—Some 2,000 backs have been measured, and the following points noted: (1) The average male high run is 15 to 15½ in. (2) The average female high run is 14 to 14½ in. (3) Numerous female backs are longer than males. (4) A girl of 13 may have an adult-sized back. (5) The maximum difference I have so far recorded in the average adult is 8 in. between the extremes. (6) Sex does not influence dosage.

For simplicity, in actual practice most cases are measured from the landmark the 7th cervical spine. In the majority of cases the 4th dorsal spine level mark is 4 in. lower down. Thus the 20-in. back from 7th cervical spine to the 4th lumbar space has a high run of 16 in.

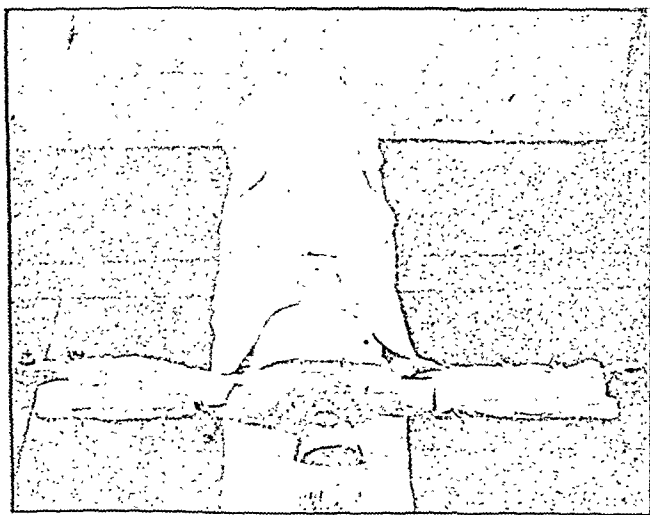
Solutions.—My experience now is limited to nupercaine and spinocaine, and I usually prefer the latter; the reason being that 1:1,500 nupercaine is not quite strong enough.

In 1934, from a certain point of view, I wrongly condemned alcoholic solutions; I still think they may not be safe when used ignorantly. Convinced that my technique was the better way of controlling alcoholic spinocaine, I began its use in February 1938 and well over 600 cases are recorded. I would stress here, that when using such a solution, details of timing, &c., must be strictly obeyed; a slightly steeper Trendelenburg 12 degrees is used for two minutes, after which the usual 8 degree operating slope is assumed. The advantages of spinocaine are seen in my statistics, e.g. in every hundred cases it constantly shows 91% of perfect spinal, as against 85% with 1:1,500 nupercaine. These very critical figures represent a score of anesthetists, including some Housemen and therefore can be improved upon by the more skilled. Nupercaine 1:2,000 successes drop to 78%. In September 1935 1:2,500 nupercaine was made for me, for babies, small children and the decrepit: A trial in over 100 adults does not recommend its routine use, with 70% success and 30% necessity for supplements. Spinocaine (novocain) has the disadvantage of not lasting out the bigger operation of one and a half hours or longer; such operations, however, should be few, e.g. perineo-abdominal excision of rectum, massive abdominal adhesions, difficult colectomies and some cases of partial gastrectomy. Intravenous pentothal, ably championed by Jarman, has easily assisted out some of the long cases; its use as an amnesic is admirable, but it must be remembered during spinal analgesia that the dose is measured in drops and not in c.c. The advantages of alcoholic spinocaine may be summed up thus; an effective, because a strong novocain solution: promotes excellent, rapid, complete mixing in its vigorous spread, during ascent. It is not true that the alcohol ascends and leaves the novocain behind; the small dose 1 to 2 c.c. is more controllable for exact block levels; its effects pass off more rapidly than nupercaine, a great advantage as well as a disadvantage; it is more useful in unilateral spinal owing to the greater divergence of its specific gravity from that of the cerebrospinal fluid; nerve block is more rapid. At the present time I use nupercaine for long operations, spinocaine for the shorter and most other cases, for unilaterals and patients requiring very accurate block limits. My preference to-day would be for a small dose say 4 c.c. of a strong hypobaric alcoholic nupercaine solution. Unfortunately in wartime I have been unable to get this prepared and hoped to have had some experience by now. I first warmed the ampoules (unnecessary for alcoholic solutions) in 1925 when using stovaine. Ampoules and syringes are now kept in an acidified water bath temperature 110°F. The rapidity of cooling is remarkable. If the interval between the removal of the ampoule and injection into the patient be two minutes, the temperature will have fallen to subnormal. For years I have prohibited

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Five solutions were used in these cases, but the great majority are concerned only with the three percaine and spinocaine. Different solutions were often used on one individual. The results show quite clearly: (1) That repeated careful spinal analgesia has done no harm to the nerve tissue. (2) That a failure, or imperfect case, can be followed next time by a perfect result; and indeed the perfect result may follow the use of the weaker solution. Convincing proof is therefore recorded here of the failure at times to introduce the dose into the C.S.F., partially or completely. It is a further argument also against the existence of rhachi-resistance.

Complete failures over the whole series amount to 2%, but only 0.5% in the last 400 cases. Such cases must be due to entire extradural injection. Imperfect cases are undoubtedly due to the whole dose not being received into the C.S.F.; some may possibly be due to spills extradurally; others to the fouling of the arachnoid. Blunt needles; blood drips and slow drips, if not rectified are prone to give rise to a percentage of imperfect results. A more successful puncture is obtained by corkscrewing the needle further into the canal, in the 3rd or lower space only, for 2 or 3 mm. should a slow drip appear. I have seen a needle block through not using a stilette. In four cases of failure after successful puncture and injection, the patient was sat up again and repunctured in the theatre and in all of them perfect spinal blocks were obtained. In a baby of 7 weeks with hypertrophic pyloric stenosis, I failed to get a result after two good punctures and injection of $2\frac{1}{2}$ c.c. of 1:2,000 nupercaine; the third attempt was eminently successful. No further proof is needed that the operator, not the patient, is at fault as a rule.

It is easier to draw off C.S.F. than to insert a solution, through the same needle, into the subarachnoid space.

Unilateral block.—I have for some years when operating on one lower limb, attempted such a block. A strict and true unilateral anaesthesia must be nearly impossible to obtain for more than twenty to thirty minutes and then only if the lateral position is retained throughout the operation. If the patient's position is altered in say ten, fifteen or twenty minutes, and even longer, from lateral to dorsal, then, within a short while, the opposite side will be similarly blocked. The solution used must be of very different sp. gr. from that of the C.S.F. Spinocaine here is very useful and I am now able to block a foot, a leg, lower thigh or the whole thigh, by timing, in the lateral position with the table sloped head up 12° . For instance, this angle for sixty seconds before putting the head down, will block the whole lower limb using $1\frac{1}{2}$ c.c. spinocaine. Yet the same dose will produce a high spinal in thirty odd seconds in the vertical position. It might seem at first that this denies my statement that the vertical position is a slow method of ascent. In 1932 and 1933 I conducted numerous experiments and learnt that as the angle of upward inclination increases, so the rate of ascent of a solution is hurried. From 45° to 60° the climb is very rapid, twice as quick as in the vertically upright position. The more acute angles allow a very slow ascent. I mention these points here because I have found them anything but clear in the minds of anaesthetists, when discussing the subject. In a retained lateral position solutions take much longer to become absorbed: the greater the difference in specific gravity the longer the fixation time.

Deaths.—I have had no deaths on the table. In a series of 14 moribund inoperable patients all of whom died within a few to thirty-six hours, I deliberately used a spinal block for the purpose of information; two of these died on the table and in one of the latter I had informed the coroner beforehand. My object was to find out the limits, if any, of spinal block in seriously ill patients. Most of the cases had intravenous drips and they hardly gave much anxiety and one was much impressed by the temporary well-being immediately after operation—a state which did not last as the block wore off. The two that died had no such assistance—one a late peritonitis and the other an intestinal obstruction with gangrene. The latter case could, I feel, have been saved a sudden death, had an infusion been set up and the rotted stomach tube in a small hospital been of any service: the patient drowned in her vomit. The stomach tube is part of the accessory spinal anaesthetic apparatus, as well as the intratracheal variety. With permission, another experiment was carried out on a $5\frac{1}{2}$ weeks old male, a hydrocephalic baby with hopeless spina bifida, born in the hospital. 4 c.c. of 1:2,500 nupercaine was injected into the cisterna magna and the baby kept head down and on one side. Extensive paralysis and unconsciousness was produced for about two hours. On recovery, a unilateral 6th and 7th cranial nerve palsy persisted. The child died some ten weeks later, the 6th nerve having recovered but the facial muscles were still parietic. I do not now use any premedication in a poor risk and cut it down to a minimum if used at all in the very elderly. Minute controlled doses of pentothal play a part here if required for awareness. Oxygen is used in most high spinals. Intravenous drips are of the utmost value, in addition to the stimulants of choice. Remember that emergency cases may have received $\frac{1}{4}$ to $\frac{1}{2}$ gr. morphia before admission.

Unexplained post-operative deaths are often due to an undetected high blood urea. Phlebitis, embolism and cerebral blood-vessel catastrophes, are not prevented by spinal analgesics. I have had three deaths, within the first three post-operative days, from cerebral disasters.

The following should be avoided: (1) Giving spinal analgesia in bad surroundings, with poor equipment and unclean working conditions. (2) Floating labels off ampoules; relying on a single theatre lumbar dab of iodine for the skin. (3) Using a technique without full knowledge. (4) The noisy theatre, the heavy-handed impatient, unco-operative surgeon. Discussions with a patient or within his earshot. (5) Avoid trying to push the lumbar puncture needle through the bone—it will not go and the pain is often the only thing a patient remembers the next day. The third lumbar space is the highest safe space in the adult. It is not unknown for the spinal cord to be present at higher levels and stabbed. (6) Avoid a steep Trendelenburg on the table. It is dangerous from many points of view and particularly in the elderly. (7) A lumbar cushion for the relaxed spine, on the table and post-operatively, will save many a backache. (8) The percentage of headaches will dwindle, by twenty-four hours' head-down bed slope. (9) Beware of over-premedication; post-operative vomiting is largely due to these drugs. (10) Avoid as far as possible full consciousness of the patient in the theatre. (11) On occasions, especially after a quick operation, or a poor risk, it is unwise immediately to move the patient back to the ward. In any case treat spinal cases gently. (12) The sensitivity or resistance of the respiratory centres, to drugs, loss of blood and falls in blood-pressure varies in individuals. Fractional premedication should be a rule. (13) It is unwise to mention or discuss spinal anæsthesia with patients; forbid the nurses from doing so. The patients should not know they are in the theatre in which case it matters little to them what procedures follow. Nevertheless it may be wise not to force a spinal on a knowing, objecting patient. (14) Get experienced with a sound technique before considering immediate modifications, altering dosage or methods of injection and other minor refinements which experience gathers. Knowledge is gained from much study of the books and literature, from the cadaver, skeleton and anatomy; visualize for yourself the behaviour of coloured solutions in a glass canal; then follows theatre experience and the follow-up of the patient.

Post-operative Complications

Headaches, mild, are frequent but temporary. These are not complained of by the patient, unless questioned; severe and lasting a few days 1-5%; persistent for many days—I have only seen two cases, which eventually entirely recovered. I have been much struck with the relatively larger percentage of fairly severe headaches, occurring in some of the failed spinals. For this one is able to offer no explanation.

Nerve involvement.—I have had no important nerve tissue complication throughout this series apart from ten cases of temporary diplopia, usually complained of the next day and passing off rapidly in most cases, more slowly in a few. One patient, a stutterer, had a unilateral spasticity unknown to me before operation. He stated, probably correctly, that the jerkiness of his lower limb was made worse after operation for some months. His doctor had noted no difference. It is important in the elderly male not to confuse difficulty in micturition, or even retention of urine, while in bed and due to chronic prostatic obstruction, with injury to the bladder nerve centres. I have never seen rectal or bladder trouble due to spinal block, or persisting pain, or patchy analgesia, while using nupercaine or spinocaine.

Backache.—Temporary, is not uncommon. I believe this is due almost entirely to prolonged strain of the unnatural posture of the relaxed vertebral column in the lumbar region. It is significantly more common in the aged. Its frequency has been lessened in the last six years by a lumbar pillow during and after operation. I do not use a bridge for gall-bladder operations.

Vomiting.—Though a minor occurrence, happens in 25% at least of my cases post-operatively. Fortunately it is not of the continued nauseated variety. The attacks of retching or actual vomiting are infrequent and on the whole undisturbing. It occurs usually some hours after operation long after the spinal effects have completely worn off. In my view it is dependent on whether the patient is sick with drugs or not. Proof of this is seen in the drugged patient, who is nauseated before the spinal is given, and the odd case which may be done with no premedication who is not sick. We all see a few cases attempt to vomit fifteen minutes or so after lumbar puncture and due to the fall in blood-pressure. Such scenes are short-lived and not often repeated. Pre-operative stimulants and nasal oxygen are of assistance.

The stomach tube must be ready and used in cases of obstruction, otherwise a quiet

but huge regurgitation will drown many a patient in a few seconds, as the sphincters relax and hollow viscera tone up, under the influence of the vagal overaction and sympathetic paralysis. I am not in agreement with those, who consider intestinal obstruction a contra-indication to spinal anaesthesia, unless the latter is used in ignorant fashion.

Indications for Spinal Analgesia

- (1) Specific, e.g. pulmonary disease; diabetes; liver or kidney states.
- (2) Therapeutic, e.g. sympathetic disturbances.
- (3) Type of operation, e.g. time-consuming; complicated; difficult; in the very obese; shock-producing. For a clean field; some manipulations; some emergencies; cases requiring perfect relaxation; in patients strongly objecting to general anaesthesia.

Under such headings one may give examples such as:—Smith-Petersen pin, excision of rectum, intestinal obstruction, difficult gastrectomy or colectomy, lumbar sympathetic ganglionectomy, fulgurization of papilloma of the bladder, vaginal repairs, prostatectomy (Harris), large ventral and incisional herniae, ectopic bladder excision, appendix abscess, and the burst abdomen.

- (4) Low spinal block is indicated in certain of the very young, or very aged.
- (5) Ill and aged patients; this is added to the list because so often such is desired by the surgeon or anaesthetist who seldom has recourse to spinal anaesthesia.

Contra-indications

- (1) *General*.—Refusal of patient. Very short or trivial operations. Bad working conditions. The inept anaesthetist.
- (2) *Infective*.—Lumbar skin infections. Septicæmia. Vertebral disease and deformity.
- (3) *Nervous*.—The patient subject to headaches. Suggestion of spinal disease.
- (4) *Circulatory*.—Myocardial—decompensation, weakness or coronary history. Hypertension—some cases. Severe anaemia and dehydration.
- (5) *Respiratory*.—Restricted or hampered respiratory excursions.

Statistics

Total cases 1,600. Males and females almost equally divided. Nearly one-third were private patients. 720 were high spinals (211 with spinocaine; 509 nupercaine). Spinocaine had a 6% greater percentage of success. 597 patients, or over one-third, were over the age of 60 years; 35 were over 80; and 205 over 70 years. 220 were emergency operations of which 86 were due to intestinal obstruction excluding strangulated hernia. Partial gastrectomy 26, cholecystectomy 124, nephrectomy 33, colectomy 21, excision of rectum 23, Cæsarean section 8, ectopic gestation 3, splenectomy 3. The male urogenital cases numbered 149 and the females 364, out of which there were 89 prostatectomies and 189 hysterectomies. Minor pulmonary complaints 8%. Major pulmonary disease 1%. These figures are doubled by general anaesthesia.

Nupercaine was used as follows: 1:1,500, 560 cases; 1:2,000, 295 cases; 1:2,500, 119 cases; spinocaine, 626 cases.

30 cases varying in age from 16 days to 3 years were given spinal anaesthetics for: congenital pyloric stenosis 14 cases; hernia 6; intussusception 1; megacolon 6; sympathectomy 1; partial colectomy 1; peritonitis 1.

The smallest babies weighed 3 lb. 8 oz. and 3 lb. 13 oz. The former, premature, an appendix peritonitis aged 16 days died thirty-six hours later. The latter, a congenital pyloric stenosis aged 17 days, survived and is well to-day. His brother eleven months later weighing 7 lb. also survived a similar operation. One case of megacolon had five therapeutic spinals. No case was lost directly owing to the anaesthetic and none gave anxiety on the table. Five died at varying intervals up to seven days.

Spinal Analgesia in Babies

The following points require attention:

- (1) For dosage and timing see formula table.
- (2) The greatest care, knowledge and understanding on the part of all the theatre staff.
- (3) Suitable pre-operative preparation, i.e. no premedication, tibial infusion drip and warmth. A suitably protected electric pad placed on the operating table. An arm board 18 in. by 2 in. is used to control the upper limb movements.
- (4) Use nupercaine 1:2,500 or 1:2,000. No. 16 hypodermic needle in the 4th space for lumbar puncture. It is easy to enter the spinal canal but not so simple to obtain and maintain a drip of C.S.F. owing to the wriggling baby. Extra-arachnoid solution loss is more likely than in the adult. The child is sat up on blocks on the table and held firmly by an understanding Sister.

(5) Signs of success are soon seen after timing in the vertical position and the assumption of the Trendelenburg. Within five minutes the legs become flaccid; the baby becomes quiet and often sleeps as some pallor becomes evident: the usual abdominal wall signs are manifest and the paralysis of these muscles leads to much loss of vocal volume. Loss of voice must not be interpreted here as evidence of paralysis of the diaphragm.

(6) Nasal oxygen. In some cases when a drip transfusion was not used, a stimulant was given.

(7) The advantages of spinal analgesia are evident, e.g. perfect relaxation; no gut protrusion; smallest incision; no haste; time for accurate suturing in layers; major procedures such as bowel resection assume less formidable proportions; less blood loss; better healing of wound. I have had no burst abdomens in this series of cases.

(8) Post-operative Trendelenburg, continued warmth and fluid drips are necessary precautions.

CONCLUSION

In my view properly conducted controlled spinal analgesia has some great advantages.

(1) *For the surgeon*.—It should teach him to be gentle; operations are made simpler; incisions smaller; there is less need for speed and bustle in ill cases; less need for post-operative adhesions, abdominal swabs and rough retractors. Certain operations are offered better advantages.

(2) *For the patient* the post-operative recovery is more smooth, for which many are grateful, who are in the position to compare.

(3) *The nursing staff* once they have got used to spinals agree that they require less post-operative attention.

(4) *The anaesthetist* in many cases is thankful for not being asked to push the patient. For him, a simple technique, complete control, fewest manipulations of patient, care and understanding, are all very desirable. He must, however, aim at great proficiency, in order to keep secure the position which spinal analgesia should rightfully hold.

[The paper was illustrated by lantern slides and the cinematograph.]

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Serial Spinal Analgesia

By J. ALFRED LEE, M.R.C.S., L.R.C.P., M.M.S.A., D.A.

SERIAL spinal analgesia is one of the latest links in a long chain of discoveries which commenced in 1885 when Leonard Corning (1885) a New York neurologist accidentally punctured the dura while trying to find out the effect of the application of cocaine to the spinal nerves of the dog, outside the dura. As a result of further work he named it spinal anaesthesia and suggested its use in operative surgery. August Bier (1899) introduced the method into his clinical practice as a means of producing loss of sensation of the lower extremities, and a little later the Frenchman Tuffier helped to popularize the method on the Continent. But it was not until the discovery of stovaine by Fourné in 1904 and of procaine by Einhorn in 1905 that spinal analgesia achieved any real popularity.

Just as there is no given dose of ether or pentothal sodium for a patient, so there is no given dose of procaine. Occasional patients are seen who show increased sensitivity to normal concentrations and amounts of drugs, including analgesic drugs. The reverse is also true and the so-called rhachi-resistant patient requires more than an average dose. Reasoning thus, Lemmon gave just sufficient procaine to reach to the desired level. This he maintained as long as necessary by adding subsequent small doses as they were needed. Thus one dose spinal analgesia became continuous, serial, intermittent, fractional or controllable spinal analgesia. When and if toxic symptoms developed the first thing he did was to withdraw some of the cerebrospinal fluid containing the drug. As analgesia is maintained by the concentration of the drug in the C.S.F. when that concentration falls below a certain level, the analgesia wears off. He found that the addition of 50 mg. each half-hour maintained analgesia in the average patient, while the initial dose lasted about forty minutes (Lemmon and Paschal, 1941, 1942).

The literature of the subject contains accounts of the use of various solutions. Lemmon commenced with 10% procaine in C.S.F. afterwards reducing the concentration to 5%

but huge regurgitation will drown many a patient in a few seconds, as the sphincters relax and hollow viscera tone up, under the influence of the vagal overaction and sympathetic paralysis. I am not in agreement with those, who consider intestinal obstruction a contra-indication to spinal anaesthesia, unless the latter is used in ignorant fashion.

Indications for Spinal Analgesia

- (1) Specific, e.g. pulmonary disease; diabetes; liver or kidney states.
 - (2) Therapeutic, e.g. sympathetic disturbances.
 - (3) Type of operation, e.g. time-consuming; complicated; difficult; in the very obese; shock-producing. For a clean field; some manipulations; some emergencies; cases requiring perfect relaxation; in patients strongly objecting to general anaesthesia.
- Under such headings one may give examples such as:—Smith-Petersen pin, excision of rectum, intestinal obstruction, difficult gastrectomy or colectomy, lumbar sympathetic ganglionectomy, fulgurization of papilloma of the bladder, vaginal repairs, prostatectomy (Harris), large ventral and incisional herniae, ectopic bladder excision, appendix abscess, and the burst abdomen.
- (4) Low spinal block is indicated in certain of the very young, or very aged.
 - (5) Ill and aged patients; this is added to the list because so often such is desired by the surgeon or anaesthetist who seldom has recourse to spinal anaesthesia.

Contra-indications

- (1) *General*.—Refusal of patient. Very short or trivial operations. Bad working conditions. The inexperienced anaesthetist.
- (2) *Infective*.—Lumbar skin infections. Septicæmia. Vertebral disease and deformity.
- (3) *Nervous*.—The patient subject to headaches. Suggestion of spinal disease.
- (4) *Circulatory*.—Myocardial—decompensation, weakness or coronary history. Hypertension—some cases. Severe anaemia and dehydration.
- (5) *Respiratory*.—Restricted or hampered respiratory excursions.

Statistics

Total cases 1,600. Males and females almost equally divided. Nearly one-third were private patients. 720 were high spinals (211 with spinocaine; 509 nupercaine). *Spinocaine* had a 6% greater percentage of success. 597 patients, or over one-third, were over the age of 60 years; 35 were over 80; and 205 over 70 years. 220 were emergency operations of which 86 were due to intestinal obstruction excluding strangulated hernia. Partial gastrectomy 26, cholecystectomy 124, nephrectomy 33, colectomy 21, excision of rectum 23, Cæsarean section 8, ectopic gestation 3, splenectomy 3. The male urogenital cases numbered 149 and the females 364, out of which there were 89 prostatectomies and 189 hysterectomies. Minor pulmonary complaints 8%. Major pulmonary disease 1%. These figures are doubled by general anaesthesia.

Nupercaine was used as follows: 1:1,500, 560 cases; 1:2,000, 295 cases; 1:2,500, 119 cases; *spinocaine*, 626 cases.

30 cases varying in age from 16 days to 3 years were given spinal anaesthetics for: congenital pyloric stenosis 14 cases; hernia 6; intussusception 1; megacolon 6; sympathectomy 1; partial colectomy 1; peritonitis 1.

The smallest babies weighed 3 lb. 8 oz. and 3 lb. 13 oz. The former, premature, an appendix peritonitis aged 16 days died thirty-six hours later. The latter, a congenital pyloric stenosis aged 17 days, survived and is well to-day. His brother eleven months later weighing 7 lb. also survived a similar operation. One case of megacolon had five therapeutic spinals. No case was lost directly owing to the anaesthetic and none gave anxiety on the table. Five died at varying intervals up to seven days.

Spinal Analgesia in Babies

The following points require attention:

- (1) For dosage and timing see formula table.
- (2) The greatest care, knowledge and understanding on the part of all the theatre staff.
- (3) Suitable pre-operative preparation, i.e. no premedication, tibial infusion drip and warmth. A suitably protected electric pad placed on the operating table. An arm board 18 in. by 2 in. is used to control the upper limb movements.
- (4) Use nupercaine 1:2,500 or 1:2,000. No. 16 hypodermic needle in the 4th space for lumbar puncture. It is easy to enter the spinal canal but not so simple to obtain and maintain a drip of C.S.F. owing to the wriggling baby. Extra-arachnoid solution loss is more likely than in the adult. The child is sat up on blocks on the table and held firmly by an understanding Sister.

the lumbar puncture needle, after removing the stylette from the latter. An ordinary Record adaptor in the end of the rubber tubing holds quite securely if pushed well home into the hub of the needle. Next the syringe is fixed to the mattress near the head of the patient, and after opening the tap, aspiration of cerebrospinal fluid is carried out to test the fluid continuity of the system. If aspiration is impossible the needle requires adjustment, slight rotation, advancement or withdrawal until aspiration is free. It is unwise to proceed with this method alone in the absence of free aspiration, if the operation is to exceed forty minutes in length.

Height of analgesia is now tested for, and if it is not adequate after ten minutes, a further 50 mg. is injected or an increase in the Trendelenburg tilt is produced. During the induction period a 5 degree Trendelenburg tilt is useful in mid and upper abdominal cases, and in ten minutes the procaine is fixed. Analgesia from the first dose lasts about thirty to forty-five minutes after which time a further 30 to 50 mg. are injected each half-hour or as may be needed. The additional doses take about two minutes to work. Reaction to stimuli on the part of the patient, together with muscular rigidity and dilatation of the previously contracted gut, show that the analgesia is wearing off. It should of course be the aim of the anaesthetist to forestall the appearance of these signs.

Indications

The method is more difficult technically than ordinary one dose spinal analgesia, but its use gives greater safety and increased sureness of smooth analgesia. The initial small dose makes for safety as it is in the theca during the first half-hour when circulatory changes due to the analgesia are most likely to occur. Subsequent injections do not cause the same degree of circulatory depression as the first one and procaine can always be withdrawn if toxic signs develop or if the analgesia ascends too high.

The general indications are the same as for any type of spinal analgesia, and the serial method should not be used in patients who are not considered fit for the one dose procedure. It is specially indicated when the anatomical scope or the duration of the operation are uncertain, while it is most useful in patients considered fit for a spinal but in relatively poor condition. In such cases a minimum amount of the drug is injected and its effects carefully watched, more being added if necessary. In cystoscopies, haemorrhoidectomies, &c., the extra trouble is hardly justified, while in operations which may require the patient to be moved on the table during their course, the needle may be slightly dislodged and the method is better avoided.

Procedure During Operation

During spinal analgesia I prefer to have most patients asleep and find that this is more certainly produced by small intermittent doses of pentothal sodium given when necessary, than by heavy premedication with drugs that are excreted less quickly. The average patient gets $\frac{1}{2}$ gr. of omnopon with 1/150 gr. of scopolamine, one hour before operation, and the majority can be roused from their pentothal sleep, at its conclusion.

The blood-pressure curves based on readings taken every five minutes, have not shown marked differences from those of patients operated on with one dose spinal analgesia. The blood-pressure is supported in the average case by the intramuscular injection of $\frac{1}{2}$ c.c. of methedrine given after the first dose of procaine. Intravenous saline, plasma or blood are infused when necessary, while in upper abdominal cases the continuous adrenaline drip described by our President (Frankis Evans, 1944) has been found most useful. Oxygen inhalations and the Trendelenburg position are employed in certain cases. A fairly steep slope can be given to the table if the mattress is securely strapped on, and if the kidney bridge, raised $\frac{1}{2}$ in., is made to coincide with the gap in the mattress.

RESULTS

These have been good. Lenmon and Paschal (1942) reported no deaths due to analgesia and only one case requiring supplementary anaesthesia, in 1,000 consecutive cases. In my small series analgesia has been adequate in all but five in which the aspiration test failed at some time during the operation. The use of the special needle should minimize this fault in future.

The difference of individual response to procaine is strikingly shown and it is not surprising that one dose spinal analgesia is sometimes imperfect. My records show a case of Fothergill's operation carried along for ninety minutes on 80 mg. of procaine, while a one and a half hour gastrectomy required 700 mg. The radical cure of a hernia needed 350 mg. of procaine before analgesia was high enough for the towel clips to be inserted without pain. Lemmon and Paschal (1942) quotes a case that needed 2,100 mg. for the performance of an appendicectomy.

for abdominal work and 1% to 3% for thoracic operations. Fraser (1943) was well satisfied with 1% procaine in saline, while Nicholson and his colleagues (1941) used $3\frac{1}{3}\%$ procaine and also reported their results with amethocaine hydrochloride made hyperbaric with glucose. I have used serial spinal analgesia in 350 cases and find a 5% solution of procaine in saline to be very suitable. Previously I worked with 5% procaine in 5% glucose which had a specific gravity of 1026, but I felt that in a few cases although analgesia was perfect muscular relaxation was not all that could be wished for, perhaps because the heavy solution tended to hug the posterior part of the theca, thus acting more strongly on the posterior nerve roots (Lee, 1943).

Equipment

A specially built mattress as designed by Lemmon is necessary, although methods have been reported in which folded sheets or padded shields have been used to keep the needle off the operating table. The mattress which is 5 in. thick lies on the operating table and has a cut-out part, 12 in. long beneath the lumbar spine. The section beneath the buttocks, thighs and legs is detachable from the upper part supporting the head and trunk, and is in three flexible portions so that the knees of a patient in the Trendelenburg position can be accommodated.

A lumbar puncture needle made of German silver which is flexible and has a lateral hole near the tip, has been used in America. Lemmon prefers to use 18 gauge. Unfortunately I have not been able to get any of these needles so have had to use ordinary Howard Jones' unhardened stainless steel needles. I have found 21 gauge satisfactory and only once in 350 cases has a breakage occurred. It was just below the skin surface and was removed without difficulty. It was due to movement in an unco-operative patient. These needles bend readily and are frequently bent on withdrawal. A needle once bent should not be used in this method again.

Tuohy (1944) discards the indwelling needle, substituting for it an indwelling number 4 ureteric catheter, introduced through a 15 gauge needle. Although the tear in the dura is greater with this method, no increase in the post-spinal headache rate or in other complications has been observed by him.

A piece of fine bore pressure tubing 30 in. long, which contains 2 c.c. of solution, connects the needle to a syringe placed on the pillow. A tap interposed between tube and syringe prevents any backflow of cerebrospinal fluid into the syringe.

Technique

One of the chief difficulties is the problem of turning the patient from the lateral to the dorsal position without disturbing the needle. A strong orderly who is accustomed to the technique can make a smooth turn every time, but may not always be available so a simple method which can be carried out by a single nurse without strain to herself, has been devised (Lee, 1944).

Height of analgesia is controlled as in any method of spinal analgesia by the amount of drug injected, the volume of solution, the height of the puncture, the speed of injection, and the specific gravity of the solution. Initial doses have been as follows: Perineum, 80 mg.; lower abdomen, 100 to 150 mg.; upper abdomen, 150 to 180 mg. using 5% solution of which 1 c.c. contains 50 mg. of procaine. In upper abdominal surgery when it is necessary for the procaine to reach the 4th or 5th dorsal root, there are advantages in the use of a $2\frac{1}{2}\%$ solution which allows a greater fluid volume to be used and so enables height to be more easily obtained. The addition of aspirated cerebrospinal fluid serves to dilute the 5% solution. In operations on the perineum or lower limbs, the puncture is made in the space between the 4th and 5th lumbar vertebrae; lower abdominal operations, in the space between the 3rd and 4th, while upper abdominal cases get their injection between the 2nd and 3rd lumbar vertebrae. In long-backed patients one space higher can be used, while one space lower is safer in the short-backed type. All injections are made at the rate of 0.5 c.c. per second, and of course doses are kept smaller in physically handicapped patients.

I prefer to give the first dose of analgesic solution from a separate syringe while the patient is in the lateral position. Before this is given the solution for maintenance is drawn into a 5 c.c. syringe and all air is expelled from the rubber tubing. The lumbar puncture must be technically perfect, and free aspiration into the syringe must be established. The mere dripping of cerebrospinal fluid is not good enough, and if aspiration is not free and cannot be made so, a second lumbar puncture must be made. After the initial injection the stylet is replaced in the needle. During the turn the anaesthetist has kept his hands sterile and he now connects the rubber tubing which is full of solution, to

Section of Comparative Medicine

President—H. J. PARISH, M.D.

[December 20, 1944]

DISCUSSION ON THE PRINCIPLES AND RELATIONSHIPS INVOLVED IN MEDICAL AND VETERINARY EDUCATION

Sir Henry Dale, after some introductory remarks, went on to say: The problems of pre-clinical education in the two disciplines, medicine and veterinary medicine, are largely a matter of mutual interest and concern. It is at the later stage of direct, so-called clinical education—whether clinical means literally at the bedside, or in field, kennel and byre, when the general physiological and pathological data and principles acquired in lecture-room and laboratory come to be applied to the recognition, treatment or prevention of disease—that their needs begin to diverge to an important degree, though still with many parallel stretches. I think that that will be accepted as something like a truism. I hope, then, that some attention will be paid in this discussion to such questions as whether common interests in the preclinical field can usefully be given greater effect than at present in community of curriculum, and whether the provision of teaching courses can, to any extent, be shared with advantage. The physiology which the student requires as a basis for his particular clinical studies has a special and factual basis which is largely, and a general and theoretical basis which is entirely, common to the needs of both disciplines. Physiological data, whether required as a basis for human or veterinary medicine, must be drawn from experiments carried out on animals, or from experiments requiring the intelligent co-operation of the conscious subject and therefore carried out on man. The physiology of the human brain and of the ruminant stomach make special chapters. But how much of the physiology of the human brain we owe to Sherrington's experiments on the dog! Similarly, the data of pathology, if they are to be adequate, must be drawn from the study of both human and animal material, and its broad principles and scientific basis will in any case be common to both.

There are obviously general problems which will affect the educational policies of both professions. Both will have to face the pressing problem of the rapid expansion of knowledge. Even its significant content becomes ever more difficult to comprise within the bounds of an educational course, which will enable the practitioner to start his work before he has passed the prime of his physical and mental vigour, and yet to bring to the help of his patients, and to the prevention even more than to the cure of disease, the essentials of a recent and progressive science. I have been glad to note that one aim of the Royal College of Physicians' report is to weed the curriculum of items which have been left in it by needs and traditions now obsolete. Sooner or later, I believe, both professions will have to face the problem of exempting from the full rigour of clinical training and qualification those who are marked from the outset for the advancement by laboratory research and for the special use in expert laboratory practice, or, perhaps, in preventive administration, of the knowledge which others will be trained to apply in day-to-day practice at the bedside or in the field. If and when such a dichotomy occurs, it will logically involve a closer association, perhaps eventually an actual fusion, of the training and qualification of those who approach the experimental and administrative career from the sides of human and veterinary medicine. I believe that you would find that the approach to such a fusion has been much closer already in some countries than we have yet thought possible here. I have one case in mind, in Australia, in which a distinguished pathologist of veterinary training held for years, with conspicuous success, the post of chief pathologist to one of the leading human hospitals of that Dominion, until the Commonwealth's needs for leadership in research on animal disease and nutrition recalled him to Government service in the field of his original discipline. If you look at the history of the researches which have strongly affected the advance of knowledge in the field of human disease, you can find abundant examples of the reciprocal influences of human and veterinary physiology and pathology. I need only mention the names of John Hunter and Edward Jenner to call to your minds very striking examples of this cross-fertilization. Remember, too, that Louis Pasteur, neither

Accurate placing of the solution in the subarachnoid space is important if the dosage is to be kept minimal, while Burford (1942) has shown that if care is taken to prevent diffusion and spread of solution, up to 800 mg. of procaine can be injected before the blood-pressure commences to fall, and before analgesia is adequate for a hernia operation. None of his experimental patients thus treated showed any cerebral or cardiovascular signs of procaine overdosage.

Post-operative headaches have been no more frequent after serial than after one dose spinal analgesia in my experience, and no other neurological sequelæ have been seen in this series. No deaths have occurred which could be blamed on the method of analgesia, and no case has caused any anxiety during operation, due to cardiovascular or respiratory depression.

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Mr. A. Dickson Wright said that he had found Mr. Etherington-Wilson's technique a very satisfactory one, but that it was hardly necessary for shorter novocain (spinocaine) anaesthetics. In the film shown it was felt that the risk of *Bacillus pyocyaneus* infection was incurred by the use of so much wetness. The organism lived in all tap water and most distilled water and sterile water in which nurses had such a simple faith. It also thrived in Dettol and C.T.A.B. lotions. Safety lay in dry sterilization or in taking the spinal equipment straight from a boiling sterilizer to the nearby patient.

As regards Dr. Lee's paper he felt that this complicated technique was not necessary for short cases or lower abdominal cases. He had used the method and brought the rubber tube round the loin into the abdominal field and had injected extra anaesthetic during the course of the operation.

Dr. M. D. Nosworthy stated that, in his experience with the Etherington-Wilson technique, the level of spinal block had not always become fixed as soon as the author affirmed but had been observed to rise higher subsequently on many occasions. He had also noticed that after one to one and a half hours the analgesia tended to wear off although muscular relaxation remained perfect; he suggested that this finding might be due to the posterior nerve roots having been bathed by the hypobaric solution only during the brief period of its upward ascent. He therefore considered that this spinal technique was not so satisfactory as some others for long operations. Dr. Nosworthy had noted the very large doses of procaine which Dr. Lee had found necessary for some of his patients and he questioned whether some of the drug might not have been deposited extradermally owing to displacement of the needle in these cases. He wondered whether Dr. Lee had had the opportunity of giving continuous spinal analgesia to any of these patients on a second occasion and, if so, whether a similarly large dose had again been found necessary.

Dr. R. Jarman said that he had used Mr. Etherington-Wilson's technique ever since its inception and he had no criticism to offer; he could not understand why various users had so many failures if they did as they were advised. The development of the technique was due entirely to Mr. Etherington-Wilson.

With regard to spinals for children, Dr. Jarman felt that in expert hands it was a very valuable anaesthetic. On the subject of Trendelenburg position he pointed out that he had done a large number of cases, mainly abdominal perineals, when the fullest possible Trendelenburg had been used with no untoward results, and he did not look upon it as such a serious factor as Mr. Etherington-Wilson suggested when he stated that 8 degrees Trendelenburg was all that was required.

The only criticism he offered on Dr. Lee's paper was that he (Dr. Jarman) did not work with surgeons who took over three hours for any one operation in the abdomen, and therefore he did not feel that he would have to use continuous spinal analgesia.

Dr. Lee, replying to Dr. Nosworthy, said that as the syringe, tubing and needle formed a closed system, and as the aspiration test was positive the whole time, it was most unlikely that solution had been deposited in the extra-dural space. Although several patients had had second operations under serial spinal analgesia, these included none who had required extra large doses of procaine.

In reply to Dr. Jarman, Dr. Lee said that length of time was not the only indication for this technique. There had been disasters when the estimated dose was too large, and failures when it was too small. The serial method enabled each patient to receive correct individual dosage for the production of adequate analgesia throughout his operation.

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physician nor veterinarian, but originally a mineralogical chemist, made practical applications of his new science of bacteriology and its immunological outgrowth almost entirely to diseases of the lower animals. The first definite proof of bacterial origin of a disease came with Koch's work on anthrax—a disease predominantly of the lower animals. I need not stress the intimate relationship and even practical overlap in clinical and especially in preventive administrative practice, between knowledge of human and bovine tuberculosis. A more recent example is afforded by Laidlaw and Dunkin's joint work on distemper—chosen deliberately as a subject of research introductory to a wider field of research on viruses, because, being a disease of lower animals, it could be made the subject of planned experiment, and also because of possible analogies with human influenza.

Professor J. Basil Buxton: There are five schools in the British Isles which are responsible for the training of potential veterinary surgeons. The Royal Veterinary College in London, founded in 1791, largely as a result of the sponsorship of John Hunter who, we are told, was the "life and soul of the movement"; the Royal (Dick) Veterinary College in Edinburgh, founded in 1823, by William Dick, a graduate of the London College; the Glasgow Veterinary College, established in 1862; the School of Veterinary Science of the University of Liverpool, established in 1873 as the new Veterinary College, Edinburgh, and transferred to Liverpool in 1904; and the Veterinary College of Ireland, Dublin, established in 1900. In 1844 a Royal Charter was granted to the graduates of the two veterinary schools (London and Edinburgh) forming them into a body corporate with the title of "Royal College of Veterinary Surgeons" and declaring that the practice of veterinary medicine was a profession and that the members of the college "solely and exclusively of all other persons whomsoever shall be deemed and taken and recognized to be members of the said profession or professors of the said act and shall be individually known and distinguished by the name or title of veterinary surgeon".

The Charter made provision for the government of the profession, for the examination of the students of the then existing colleges and of such other colleges as might in future be affiliated to the Royal College by Royal Sign Manual and for their admission to be members of the Royal College of Veterinary Surgeons. It is thus to be clearly distinguished from the Royal Veterinary College which is purely a teaching college and from the National Veterinary Medical Association which is an association of qualified veterinary surgeons and is akin to the British Medical Association. The functions of the Royal College of Veterinary Surgeons are analogous to those of the General Medical Council except that the Council of the R.C.V.S. has sole control of the only examinations which qualify a veterinary student to practise as a veterinary surgeon and of the examiners, external and internal, who conduct these examinations at the several teaching centres. Since 1932 the Council of the R.C.V.S. has required the veterinary, like the medical, student to complete a course of training extending over five years, in which period he has to cover a field of work similar to but in some respects wider in scope than that covered by the medical student. In 1906, the University of London created the degrees of Bachelor and Doctor in Veterinary Science and students of the Royal Veterinary College, London, who have matriculated in the University are eligible to take the examinations for these degrees as internal candidates. Students from other veterinary colleges, who have matriculated, may take the examinations as external candidates. The course of instruction, which extends over a period of five years, and may be taken concurrently with the course for the Diploma of Membership of the R.C.V.S., does not include the clinical subjects.

In 1911 the degrees of Bachelor and Doctor in Veterinary Science were instituted by the University of Edinburgh and students of the Royal (Dick) Veterinary College who have matriculated are eligible to take the examinations for these degrees. At the University of Liverpool matriculated students of the School of Veterinary Science are eligible to sit for examination for the degrees of Bachelor, Master and Doctor of Veterinary Science. The clinical subjects are included in the course of instruction for the B.V.Sc. degree. In addition to the Diploma of Membership the Council of the R.C.V.S. awards a Fellowship Diploma, a Diploma in State Veterinary Medicine and a Diploma in Tropical Veterinary Medicine and Hygiene. A Diploma in Tropical Veterinary Medicine is also awarded by the University of Edinburgh. There are in addition various postgraduate courses which are designed to give further instruction in pathology, bacteriology, preventive medicine and the clinical subjects. During the past century the field of veterinary activity has undergone several profound changes which, in general, have led to an extensive broadening of the curriculum to meet, and in some cases to anticipate, additional services to be rendered by the veterinary surgeon to the public.

The veterinary profession is and will continue to be a relatively small profession. It

may be taken that the number of veterinary surgeons in the country during the decade immediately preceding the war was economically sound from the professional aspect, and with some knowledge of the requirements over a reasonable period of time after the war there should be no difficulty in estimating the number of veterinary surgeons likely to be required to meet the public need.

The purpose of veterinary education is to train students to develop those qualities of mind and character which will fit them to enter general practice and at the same time to provide a foundation for those who may wish to specialize later.

The ideal background would doubtless be a course of study leading to a degree in Arts. A veterinary graduate cannot obtain the Diploma of Membership of the R.C.V.S. until he reaches 21 years of age and he is not admitted to the course of instruction until he is 16. When the course extended over four years the majority of students did not come up until 17 years of age or more, but since a year has been added to the period of instruction there has been a tendency for this year to be "saved" at the expense of his schooling and at a time when he can least well afford to miss it. It would be far better if the minimum age for admission to our veterinary schools were 18, for it is between 16 and 18 years of age that school life is of its greatest value in developing a boy's character, broadening his outlook on life and fostering those latent qualities of responsibility and leadership which are so necessary in later life. This is not to suggest that his time should be devoted to specialized study of the basic sciences of the first professional examination in order to pass a 1st M.B. examination or a Higher Schools Certificate in a single group of subjects and so secure exemption from the first professional. The only justifications for retaining the more fundamental sciences of chemistry, physics and biology in the veterinary curriculum are firstly to meet the need of students who have not acquired a general knowledge of them at school and secondly to present them with a definite bias in the direction of more advanced subjects of the curriculum.

The curriculum of an active profession such as veterinary medicine requires constant revision. When the veterinary course was extended to five years it was with the sole object of providing more time in which the student might assimilate the instruction which was provided for him. Unfortunately it happened that almost before the change became operative, it was seized upon by teachers and examiners as a heaven-sent opportunity to increase the amount of factual knowledge to be crammed into and expected of the unfortunate student. At present the examinations are more a test of the student's capacity to remember detail than an opportunity to exhibit his expression of those principles and methods which are the essential basis of his professional life.

Any tendency to specialize within the pregraduate curriculum is to be deprecated. The nature and extent of the subjects, their relative importance and co-ordination and the type of instruction to be given should be determined by the needs of general practice. In this way only can a sufficiently generous and resilient foundation be laid upon which the future practitioner, teacher, research worker, or administrator may base, by means of postgraduate study, the special knowledge he will require.

In my opening remarks I made reference to the relationship between the several veterinary schools and the R.C.V.S. on the one hand and their adjacent universities on the other. There has for long been a feeling that veterinary education is too far divorced from the universities and that the nucleus for collaboration which has been in existence for a number of years has failed to achieve the object for which it was designed. When I undertook the Principalship of the Royal Veterinary College after thirteen years of university life I was not unmindful of the desirability of as close collaboration as possible with the University of London. The college was already recognized by the university and most of the teaching staff who were engaged in preparing students for the veterinary science examinations were "recognized teachers" of the university. Valuable contacts had been established between many of the members of the teaching staff who were also engaged in research and workers in other schools of the university who were interested in related problems. The Students Union Society of the college was affiliated with that of the university and our students participated fully in their organized games. Indeed certain of them were captains of the university clubs. Later, arrangements were made whereby students of the college had the privilege of residence in university hostels and licensed lodgings. It was hoped that in this way a really effective liaison might be established between the students and staff of the college and their opposite numbers in other schools, notably the medical schools of the university. Whilst much has been achieved in this direction the chief impediment in the way of developing the desired degree of co-operation in policy and activities has been the small number of students that could be induced to read for the university degree in veterinary science. This reluctance to take the concurrent courses is not on account of the extra expense but

because the student whose objective is usually general practice, cannot be induced to see the worth-whileness of the extra labour involved. I do not see any prospect of a development along these lines sufficient to effect a really close liaison. At the same time I am convinced that the veterinary profession will not establish fully the chain of vocational fraternity with medicine on the one hand and agricultural science on the other unless the first links are forged in a youthful environment common to all.

No other professions are so closely connected as are those of medicine and veterinary medicine, and no one will question the desirability of a yet closer active, natural liaison within the framework of some educational scheme.

It would not be possible, even if it were shown to be desirable, to teach medical and veterinary students in the same classes for although it might be practicable for a part of the subjects of the first year to be so dealt with, beyond that stage the special requirements and wider scope of the veterinary course make it necessary to provide special classes and specially trained teachers. The desired results could, however, be secured through an administrative system which enabled medical and veterinary students to make free use of the courses of instruction given in each discipline. By such means their youthful curiosity would be awakened and the natural desire for further information would be stimulated.

Professor G. W. Pickering: The need for improved veterinary and health services has been recognized by the Government and the recent Loveday and Goodenough Reports recommend considerable increase in the facilities for veterinary and medical education, and in the financial aid which they receive from the State. The Goodenough Report makes the important recommendation that increased financial support should be conditional on a reform of the medical curriculum.

The dilemma of medical education, and I suspect also of veterinary education, is the choice between sacrificing the educational or the vocational needs of the student. For on the one hand we propose to give these students a university education, and on the other, we propose to train them to be masters of a craft. At the present we achieve neither. Several solutions of this dilemma have been proposed. It has been suggested that we should cease to attempt a university education for the average student, giving him a much simpler and more practical training in the craft of medicine and reserving an improved and more truly educational university course for a select few, who shall become the research workers and consultants of the future. I doubt if it is either wise or practicable in human society to borrow method from the bee and select workers and queens at the outset in order to nourish them suitably for their future functions. I am sure the workers would be jealous of the queen. Moreover we all know potential queens who have turned out to be second-rate workers, and potential workers who have developed into queens. The medical curriculum should be divided into two phases, *undergraduate* and *postgraduate*. The postgraduate period should pay particular attention to vocational needs; it should provide a practical training in the craft of medicine, and for the requirements of specialists. It should begin with a year's resident hospital appointment, to be made compulsory for all who intend to practise medicine. It should proceed with the requisite training and appointments for those who intend to specialize. The proper organization of postgraduate education is the first step to freeing the undergraduate curriculum from its present intolerable load.

This done, the reform of the undergraduate curriculum should be much simpler. The essential point about the undergraduate period is that it should provide an education in the true sense of the word. It should seek to train the student to use his mind, utilizing material that is proper to the understanding of normal and diseased man. The task is not easy. The true proportions of the problem may be conveyed by reminding you that the unfortunate medical student has to pass through the following university departments: Chemistry, Physics, Botany, Zoology, Anatomy, Embryology, Physiology, Biochemistry, Pharmacology, Bacteriology, Pathology, Chemical Pathology, Medicine, Surgery, Obstetrics, Gynæcology, Pædiatrics, Public Health, Forensic Medicine, not to mention the various specialities. Since each of these departments duly demands of the student its pound of flesh, it is no wonder that our medical students become little more than memorizers, who spend their days attending classes and their evenings in reading textbooks which, once the appropriate examination is behind, are never opened again. How are we to preserve in such a course the elements of a university education?

The first need is for co-ordination. At the present time there is a growing tendency for departments to conduct their courses with little reference to what is going on at the same time in other departments, and with still less to what has preceded and what is to follow. Thus in the preclinical period, the student may learn about the structure of the gut from the anatomist during one term, its movements from the physiologist in

another term, and the digestion and absorption of food from the biochemist in a third. The lack of co-ordination is at least as great in the clinical years. The result is to confuse the student and to increase enormously the difficulty he has in understanding. Knowledge is, after all, continuous, and its subdivision is a convenience to the teacher and investigator, but a hindrance to the student. The remedy is a strong-minded dean who will see that courses are planned with the primary object of creating unity.

The second need is for the elimination of unnecessary matter from the curriculum. The overloading of the curriculum has proceeded relentlessly because the principle has been applied of including for obligatory study everything which could be considered as useful to certain aspects of medical practice. In the future a different principle must be applied; subject matter should be eliminated unless a strong case can be substantiated for its retention. Matter which is essential for only some branches of medical practice should be ruthlessly transferred from the undergraduate to the postgraduate curriculum. In deciding what matter to retain two considerations should be given special emphasis. The first is that the matter is necessary for the exposition of method. Karl Pearson's words: "The true aim of the teacher should be to impart an appreciation of method and not a knowledge of facts", remind us that method is retained as an attitude of mind long after facts have been forgotten. The second consideration is that the matter is essential to the proper understanding of phenomena that occur frequently in health and disease, or in the jargon of the day, to the understanding of fundamental principles.

These few remarks on a very difficult subject have neglected three important points, namely, the necessity for a revision of teaching methods, the reform of the examination system in conformity with the curriculum, and the recruitment and selection of students. The kind of man who is attracted to veterinary or human medicine is determined by the kind of life to which he looks forward when he is qualified, and will determine the standard of professional practice in the future. This is the strongest argument for giving the professions a responsible share in the planning and control of the services of which they will form the living elements.

Dr. D. McClean gave an interim report of the views of a committee of medical scientists most of whom were actively engaged in preclinical or clinical teaching. He called attention to the excellence of the principles enunciated by the Goodenough Committee but regretted their failure to implement these in their recommendations, notably in relation to the pruning of the curriculum. Medical education was in a chaotic state, including, as it did, a medley of material, partly in the hope of fulfilling vocational needs and partly to provide a scientific training. Students were given a smattering of many sciences and reached a university standard in none. The 2nd M.B. examination was regarded as a *pons asinorum* bearing little relation to the student's real interests. Dr. McClean outlined some of the constructive suggestions put forward by the committee and said that they had been reluctantly compelled to drop the idea of two separate courses, one for those intending to practise medicine and the other for those desiring to teach or do research; they were now inclined to favour the development of a greater elasticity of the curriculum as the course proceeded and to remodel examinations so that these were designed to find out what a student knew and was interested in rather than what he did not know.

Dr. Fred Bullock, Secretary, R.C.V.S., said he had been glad to be present at a meeting at which veterinary surgeons could hear criticisms of the medical curriculum. It would perhaps correct their impression of the relative imperfections of the veterinary curriculum. One advantage which the veterinary profession was unique in enjoying was that twice a year, after each tour of the examiners appointed by the college, during which they met the internal examiners and discussed problems with them, their reports were submitted to the council of the college, and their criticisms and suggestions considered.

Professor O. G. Edholm: The complaints made about teaching in veterinary and medical schools ignore the fact that the teachers both enter and are selected on the basis of research work. A period of training in teaching methods is essential: a corollary being the greater expansion of research posts. Pruning of the curriculum is a difficult task which calls for the help of educational psychologists, who could also assist in plans for the co-ordination of the different parts of the course.

The overlap of the medical and veterinary course in the preclinical stage means that a fundamental course in physiology could be taken in common, provided that the emphasis at this stage is not placed on human physiology.

Dr. John Rickman made two points: (1) The best way to solve the difficulties which arose when "pruning the curriculum" was to make a job-analysis of the daily work of the practitioners (medical and veterinary), i.e. to base the new training programme on experience instead of on "adjustments" between different bodies of interested parties in

the teaching world. This would also help us to know better how much attention to give to social and psychological medicine, which were relatively neglected in the present teaching. (2) Human and veterinary medicine had some things in common but the over-riding fact was that the patient population belonged in the one case, but *not* in the other, to the same species as the practitioners. When the medical practitioner began to study his functional relation to the community of which he was a member he would be helped in solving difficulties not only in the planning of the curriculum of students but also in the social relation of the profession to the community.

Dr. J. T. Edwards reviewed the early history of the London and Edinburgh veterinary colleges and showed how the facts supported the thesis propounded by Sir Henry Dale that a dichotomy is now called for between training for the essential craft of medicine and training for research, and, maybe, administration. The fundamental principle appeared to be to turn out craftsmen sufficiently versed in their craft to perform satisfactorily the demands ordinarily made on them by the public, sufficiently educated to be able to adjust their methods wisely to changing conditions and yet not so much over-educated in non-essentials that they would disdain the current work ordinarily demanded of them. It had not been so much the rarity of teaching talent but the faulty selection of teachers and the same held to-day for some other professions, men being chosen for their administrative capacity or other reasons wholly estranged from their specific professional capacity. Dr. Edwards criticized what he considered the unsatisfactory methods adopted by official committees in conducting inquiries, failing usually to trace the problem to its roots by historical study and committing themselves to the expression of ideals rather than performing what was sociologically sound, namely, a proper "job-analysis".

He would like to pay the tribute which Sir Henry Dale deserved on what was a historic occasion, namely, the first time a President of the Royal Society had made an Address on the subject of veterinary education since his great predecessor Sir Joseph Banks (who presided from 1778 onwards for forty years) took a leading interest in the movement which eventually brought about the establishment of veterinary education in this country in 1791. John Hunter, a contemporary, was also the "life and soul" of the movement.

Dr. E. G. White agreed with Professor Buxton that the veterinary curriculum was in need of considerable pruning, especially in some subjects in which a mass of descriptive detail was taught. The method of conducting some of the examinations also needed to be reviewed so that more time was made available for determining the practical ability of students, particularly when dealing with the *living animal*. The basic veterinary training should be one that best fitted a man or woman for general practice and as many graduates as possible should be encouraged to proceed to a further course of study. The basic qualification might be a diploma, as at present, or a degree: postgraduate qualifications would include the various diplomas already established and also perhaps an Honours Degree taken in one subject, with maybe one or more subsidiary subjects. This latter course of study would provide veterinarians with special training enabling them to undertake research in veterinary colleges and research institutes and in the field. The present B.Sc.(Vet.Sci.) did not fill this want because it required a somewhat higher standard in several subjects rather than a special knowledge of any one subject and because clinical subjects were not included.

Dr. W. R. Wooldridge stated that whereas medicine had many centres of instruction varying above a common minimum standard, veterinary education was governed by one examination. It was becoming increasingly difficult in view of the total length of this examination, the difficulties of travel for examiners, their rushed periods for marking and the differing facilities at individual centres to claim this as a uniform examination. But it did tend to arrest individual developments at the schools. The university medical schools were not those which gave the poorer instruction. They had in fact produced many stimulating teachers and research workers, including clinicians, who had markedly influenced medical progress. Veterinary education was unlikely to benefit similarly until its whole course, including medicine and surgery, was afforded the same opportunities and facilities.

The President thought that insufficient care was sometimes taken in the selection of professors, who might be outstanding research workers but bad teachers. Lectures to students were not always as useful as they might be, owing to the inability of the lecturer to impart instruction. School teachers received expert tuition in teaching, but university professors had no such training and might never acquire proficiency. A further important point was that, as professional men were expected to take a leading part in local affairs, "culture as well as clinics" must be prominent in their education.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[October 19, 1944]

? Eosinophilic Granuloma. ? Sarcoid of Boeck.—J. E. M. WIGLEY, M.B.

Mrs. E. C., aged 46. Two years ago a lesion was excised from her forehead at Kingston Hospital. She says the present lesions appear to her the same, and have developed since. On the forehead and nose are some three to four discrete, greyish-brown, infiltrated lesions, varying in size up to that of a silver threepenny piece. (See fig.) They are slightly raised above the surface, smooth to the touch, and on diascopy leave a greyish-brown staining. Otherwise physical examination is negative.

W.R. negative. Mantoux test: 1:10,000 strongly positive. Control negative.

Blood-count: Total W.B.C. 7,200 per c.mm.; polys. 68%; eosinos. 4.5%; basos. 1.5%; lymphos. 21%; monos. 5%.

X-ray examination: Chest, hands and feet negative.

Histology (Dr. I. Muende).—The corium contains numerous coalescing foci of closely packed cells, among which there are numerous endothelial cells, some binucleate, very numerous eosinophils, polymorphs and a few plasma cells.

No acid-fast bacilli seen in Ziehl-Neelsen preparations. *Chronic infective granuloma of the skin*. Not suggestive of sarcoid (Boeck).

The clinical appearances of these lesions seem to me almost typical of sarcoid of Boeck, which the histology can hardly be said to be.



? Eosinophilic granuloma. (Photograph by Dr. A. C. Roxburgh.)

Dr. W. Freudenthal: Dr. Wigley's section shows a very unusual picture. Chief features are reticulo-endothelial cells (histiocytes) and large numbers of eosinophilic cells, some of which show phagocytic activity (Burkhart and Montgomery, 1944). The eosinophilic

the teaching world. This would also help us to know better how much attention to give to social and psychological medicine, which were relatively neglected in the present teaching. (2) Human and veterinary medicine had some things in common but the over-riding fact was that the patient population belonged in the one case, but *not* in the other, to the same species as the practitioners. When the medical practitioner began to study his functional relation to the community of which he was a member he would be helped in solving difficulties not only in the planning of the curriculum of students but also in the social relation of the profession to the community.

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The President: Has this patient had necrotic lesions?

Dr. Theresa Kindler: There was an acute varicella-like eruption but it subsided in three weeks. As he had no fever I presumed it was an acute phase of the disease.

Dr. Dowling: Is it the general impression that pityriasis lichenoides chronica has become less common than it used to be in comparison with the number of more acute types?

Dr. J. E. M. Wigley: Is not this disease also known as parapsoriasis by French dermatologists?

The President: I regard it as a variety of the parapsoriasis group.

Dr. Wigley: I have heard parapsoriasis described with considerable justification, in my experience, as a superficial scaling eruption entirely unaffected by any form of treatment.

Multiple Rodent Ulcers.—ENID M. GLEN, M.R.C.S., L.R.C.P.

Mrs. A. W., aged 72. Ten years ago a small nodule appeared on the abdomen, gradually increasing in size which often bled. This was treated seven years later by the insertion of five radon seeds for four days.

Six months later an ulcer developed on the abdomen, $1\frac{1}{2}$ in. \times 1 in., also two other small ulcers. Radium plates applied. Dosage: 864 mg.hrs.; 576 mg.hrs.; 1,248 mg.hrs.

Biopsy report: Basal-celled carcinoma, suggesting beginning of squamous prickle-celled growth; not definite.

Six years ago some pigmented patches on trunk up to 1 cm. diameter. On abdomen, one large rodent ulcer $1\frac{1}{2}$ in. \times $1\frac{1}{4}$ in. and two small confluent ulcers each $\frac{1}{2}$ in. diameter.

Treatment.—(a) 8 radon seeds 16.7 millicuries for five days. (b) 10 seeds 17.8 millicuries inserted deeply under ulcer for five days.

The President: The biopsy was from the lesion on her abdomen? It was squamous in one part and basal in another?

Dr. Enid Glen: The report states that it was not definite but suggests prickle-celled carcinoma.

The President: That was six years ago and although it has had no treatment it has not invaded the abdomen.

Dr. G. B. Dowling: Flat basal-celled carcinomata have a certain tendency to become squamous and to prove ultimately fatal. This has happened within my experience on several occasions, and I feel that there is a strong case for advising a complete excision, and skin graft when necessary, for this condition rather than any other treatment, such as freezing or radiotherapy.

The President: Do you think that applies to the multiple type or to flat ones of any sort?

Dr. Dowling: To flat ulcers of any sort.

The President: I have seen several which developed a squamous epithelioma in the middle. I favour excision if the situation is a convenient one.

Dr. A. Burrows: Multiple rodent ulcers or basal-celled carcinomata of body and limbs are curiously unsatisfactory from the radiotherapeutic point of view. Even when there appears to be local cure, and it is not the rule, often recurrence appears at the same site. I am of the opinion that one should find some other more satisfactory method of treatment or technique; certainly excision should be considered. This patient will have another section done. I always thought a notable proportion of rodent ulcers showed squamous-celled changes. Dr. Henry MacCormac (*Middlesex Hospital Cancer Reports*, 1910, 19, 172), showed this to be the case, so that one would expect to find them in these cases as well as in others.

Dr. W. N. Goldsmith: I agree with Dr. Burrows. I have seen a case with an enormous number of these carcinomas which have all responded very well to CO₂ snow, even those which had a bump in the middle; as a rule they do not do at all well with X-rays or radium, which produce atrophy and telangiectasis with lower doses than usual. One often finds prickle-cell growth in some parts. That is not necessarily alarming. One elderly woman had a quite frank prickle-celled epithelioma of the whole cheek, which at first I thought was a gumma; eventually it ulcerated right through to the mucous membrane, yet there were no enlarged glands and no metastases.

Dr. G. B. Dowling: I agree that these cases are resistant to irradiation. Quite recently I had charge of an old psoriatic who had had arsenical treatment years before, and who had a large number of these flat epitheliomata of which some were perhaps already squamous, the most important were treated with X-ray without effect, and within a short period he died of carcinomatosis.

Superficial basal-celled epitheliomata we used to 1,000 to 1,500 r. repeated two to five times

cells are arranged in foci or are diffusely scattered amongst the reticulo-endothelial cells. The picture reminds me of that found in "Eosinophilic Granuloma (Eosinophilic Reticulo-endotheliosis) of Skin" (Martinotti, Nanta, Pasini, Cerutti). It may be that this case is an instance of this very rare disease (or body reaction?), about the clinical manifestations and pathogenesis of which we still know very little.

In 1940, both Otani and Ehrlich, and Lichtenstein and Jaffe, independently, described a condition with an identical histology in the bone. Farber (1941) suggested that this "Eosinophilic Granuloma of Bone" was a variant of Schüller-Christian's disease, a view accepted by T. B. Mallory (1942) in a critical review on this subject. These authors were unaware of the "Eosinophilic Granuloma of Skin".

It might be worth while to search in Dr. Wigley's case for any symptoms of Schüller-Christian's disease (X-ray of bones, sections stained for fat, &c.).

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Dr. I. Muende: The sections were not stained for fat, for nowhere could one see anything suggestive of a foam-cell, or an endothelial cell with any obvious vacuolation.

The diagnosis of eosinophilic granuloma came to my mind, but the eosinophils were not as numerous in the section, nor was there the high degree of eosinophilia associated with the latter disease. I could not accept the diagnosis of sarcoid, and considered it much more likely that we were dealing with a case of Hodgkin's disease with skin lesions.

Dr. H. C. Semon: It occurs to me to comment on the strongly positive Mantoux test in this case.

The President: The patient had no tuberculous lesion?

Dr. I. Muende: No.

Dr. A. Burrows: If this granuloma is similar in type to the tumours in the Christian-Schüller syndrome it should be radiosensitive and this fact might be helpful in diagnosis.

Dr. J. E. M. Wigley: The X-ray of the chest showed a certain amount of most of the ribs; there was no obvious change in the bones.

The President: I understand skiagrams of the hands and feet were normal?

Dr. W. N. Goldsmith: Were the earlier lesions more lumpy?

Dr. Wigley: They are now, if anything, a little more lumpy than when I first saw them.

Dr. Goldsmith: The flatness is more like xanthoma than Hodgkin's disease, and perhaps the colour also.

Pityriasis-Lichenoides Chronica (Parapsoriasis Guttata).—THERESA KINDLER, M.D. (for A. BURROWS, M.D.).

N. L., 8-year-old boy, has had a non-irritating, slowly spreading rash on his trunk, buttocks and the proximal parts of his extremities for five years. The eruption consists of pin-head to pea-sized maculo-papules with very little infiltration; they are pink or reddish at first, some are covered with a thin scale. Later they become greyish-brown; the scale can be detached as a whole and has a lid-like, mat appearance. When removed, it leaves a moist surface or may show some bleeding but not of the papillary type. Finally, the subsiding lesion leaves only a grey easily removable scale. New lesions crop up continuously as some of the old ones subside. In some places coalescence of the lesions forms larger, superficial scaling patches. The eruption has been completely unresponsive to treatment, including ultraviolet irradiation.

Dr. Forman: Could we have an opinion as to the natural course of this disease? How long does the rash take to disappear?

Dr. T. Kindler: Cases have been known to last twenty years.

The President: I remember a boy who had the more necrotic type, the so-called varioliformis type, which cleared up after a year or two. I have seen during most of the war period a soldier who goes on more or less continually with the eruption. It is reduced by ultraviolet light but does not get well.

Dr. G. B. Dowling: I recall a case of what we are nowadays accustomed to calling pityriasis lichenoides acuta upon whom during the course of at least a year, every variety of treatment which has been said to influence the condition was tried in turn. Ultimately the patient and I agreed to give it up. Several months after the cessation of treatment the rash disappeared.

The President: Has this patient had necrotic lesions?

Dr. Theresa Kindler: There was an acute varicella-like eruption but it subsided in three weeks. As he had no fever I presumed it was an acute phase of the disease.

Dr. Dowling: Is it the general impression that pityriasis lichenoides chronica has become less common than it used to be in comparison with the number of more acute types?

Dr. J. E. M. Wigley: Is not this disease also known as parapsoriasis by French dermatologists?

The President: I regard it as a variety of the parapsoriasis group.

Dr. Wigley: I have heard parapsoriasis described with considerable justification, in my experience, as a superficial scaling eruption entirely unaffected by any form of treatment.

Multiple Rodent Ulcers.—ENID M. GLEN, M.R.C.S., L.R.C.P.

Mrs. A. W., aged 72. Ten years ago a small nodule appeared on the abdomen, gradually increasing in size which often bled. This was treated seven years later by the insertion of five radon seeds for four days.

Six months later an ulcer developed on the abdomen, $1\frac{1}{2}$ in. \times 1 in., also two other small ulcers. Radium plates applied. Dosage: 864 mg.hrs.; 576 mg.hrs.; 1,248 mg.hrs.

Biopsy report: Basal-celled carcinoma, suggesting beginning of squamous prickle-celled growth; not definite.

Six years ago some pigmented patches on trunk up to 1 cm. diameter. On abdomen, one large rodent ulcer $1\frac{1}{2}$ in. \times $1\frac{1}{4}$ in. and two small confluent ulcers each $\frac{1}{2}$ in. diameter.

Treatment.—(a) 8 radon seeds 16.7 millicuries for five days. (b) 10 seeds 17.8 millicuries inserted deeply under ulcer for five days.

The President: The biopsy was from the lesion on her abdomen? It was squamous in one part and basal in another?

Dr. Enid Glen: The report states that it was not definite but suggests prickle-celled carcinoma.

The President: That was six years ago and although it has had no treatment it has not invaded the abdomen.

Dr. G. B. Dowling: Flat basal-celled carcinomata have a certain tendency to become squamous and to prove ultimately fatal. This has happened within my experience on several occasions, and I feel that there is a strong case for advising a complete excision, and skin graft when necessary, for this condition rather than any other treatment, such as freezing or radiotherapy.

The President: Do you think that applies to the multiple type or to flat ones of any sort?

Dr. Dowling: To flat ulcers of any sort.

The President: I have seen several which developed a squamous epithelioma in the middle. I favour excision if the situation is a convenient one.

Dr. A. Burrows: Multiple rodent ulcers or basal-celled carcinomata of body and limbs are curiously unsatisfactory from the radiotherapeutic point of view. Even when there appears to be local cure, and it is not the rule, often recurrence appears at the same site. I am of the opinion that one should find some other more satisfactory method of treatment or technique; certainly excision should be considered. This patient will have another section done. I always thought a notable proportion of rodent ulcers showed squamous-celled changes, Dr. Henry MacCormac (*Middlesex Hospital Cancer Reports*, 1910, 19, 172), showed this to be the case, so that one would expect to find them in these cases as well as in others.

Dr. W. N. Goldsmith: I agree with Dr. Burrows. I have seen a case with an enormous number of these carcinomas which have all responded very well to CO₂ snow, even those which had a bump in the middle; as a rule they do not do at all well with X-rays or radium, which produce atrophy and telangiectasis with lower doses than usual. One often finds prickle-cell growth in some parts. That is not necessarily alarming. One elderly woman had a quite frank prickle-celled epithelioma of the whole cheek, which at first I thought was a gumma; eventually it ulcerated right through to the mucous membrane, yet there were no enlarged glands and no metastases.

Dr. G. B. Dowling: I agree that these cases are resistant to irradiation. Quite recently I had charge of an old psoriatic who had had arsenical treatment years before, and who had a large number of these flat epitheliomata of which some were perhaps already squamous, the most important were treated with X-ray without effect, and within a short period he died of a generalized carcinomatosis.

Dr. Theresa Kindler: For the multiple superficial basal-celled epitheliomata we used to employ Grenz rays in Vienna, in doses of 1,000 to 1,500 r, repeated two to five times at four weekly intervals.

Dr. W. N. Goldsmith: I have never used Grenz rays in the treatment of multiple cancers.

The President: I have frozen a number of them but I have not been pleased with the results. I always get the lesions excised if I can, though Dr. Finzi has cured a number for me with screened radium.

Two Cases of Multiple Arsenical Cutaneous Carcinomata.—BRIAN F. RUSSELL, M.D., and ROBERT KLABER, M.D.

CASE I.—Mrs. J. F., aged 53, has been treated for epilepsy for thirty-two years.

History.—From 1912 to 1924 she received a bromide mixture, containing liquor arsenicalis, m iii , t.d.s., and for a month in 1935, m i , t.d.s.: an intake of over 37,000 minims in twelve years.

In February 1944 she noticed an ulcer on the right side of her chest, which enlarged and became painful.

Condition on examination (9.2.44).—Dark-haired woman with skin showing polymorphic lesions:

(1) One inch diameter button-like, raised indurated ulcer with hard raised rolled edge and slough in floor, on right side of thorax (section shown). This lesion has since been excised.)

(2) One inch diameter, circular, slightly raised plaque with central crusting and marginal pearly telangiectatic edge over the sternum, with smaller similar lesion adjoining.

(3) Multiple seborrhœic warts on trunk.

(4) Multiple small mollusca fibrosa around neck.

(5) Multiple pigmented macules on trunk.

(6) Several de Morgan's spots.

There is no "raindrop" pigmentation and there are no palmar or plantar keratoses.

Section from lesion on side of thorax shows a squamous-celled carcinoma with active mitoses.

Progress.—Several fresh lesions have appeared on left breast, right side of chest, right thigh, left shoulder and lumbar region. These range from small pearly nodules to larger plaques with raised, pearly, serpiginous edges and central scabbing or atrophic telangiectatic scarring.

CASE II.—Miss A. L., aged 44, has been treated for epilepsy for thirty-one years.

History.—From 1913 to 1934 she received a bromide mixture, containing liquor arsenicalis, m iii , t.d.s., and from 1934 to 1943, m i , t.d.s. This represents a total intake of 79,000 minims, or just over one gallon, of liquor arsenicalis in thirty years, equivalent to a little over 700 grains of arsenic trioxide.

About fifteen years ago, during a fit, she cut herself with her corsets in the right lower abdomen. The resultant sore did not heal but formed a scabbed surface, with periodic shedding and reforming of the scab, with bleeding.

Two years ago a fresh lesion appeared between the breasts and others have been forming ever since.

Condition on examination.—Dark-haired woman with skin showing the following lesions:

(1) $1\frac{1}{2}$ in. diameter heavily crusted indurated erythematous plaque in right iliac fossa.

(2) Split-pea-sized nodule adjoining right nipple (section).

(3) Multiple plaques up to $\frac{3}{4}$ in. diameter on shoulder, chest, thigh, &c., consisting of annular lesions with raised pearly rolled edges and central atrophic scarring.

(4) Many mollusca fibrosa around neck.

(5) Many seborrhœic warts on trunk.

(6) Early keratinous changes on palms, with a few pin-head-sized keratoses.

There is no "raindrop" pigmentation.

Section from lesion adjoining nipple shows multiple basal-celled carcinoma with marked cystic degeneration.

The President: These are very interesting cases and should make us doubtful about adding the traditional liquor arsenicalis to bromide mixtures. In what proportion of cases does it prevent bromide eruptions? Why are some of the growths basal- and some squamous-celled? Why are these patients not pigmented?

Dr. J. E. M. Wigley: I have seen several cases of bromide eruptions in children which occurred while they were taking small doses of arsenic with their bromide mixtures.

Dr. W. N. Goldsmith: I have seen a number of beautiful cases of raindrop pigmentation and palmar keratosis at the West End Hospital for Nervous Diseases in patients who had taken bromide with arsenic for many years. I have never seen a case of multiple carcinomatosis among that hospital population; on the other hand I have seen cases of it in persons who had not taken arsenic, so that I am not convinced of the close connexion between the two.

The President: Many of us have seen patients with psoriasis whom somebody put on arsenic many years previously without telling them to cease taking it after a time, so they took it for years and ended up with arsenical keratoses, epithelioma and of course, still psoriasis.

Dr. H. C. Semon: I remember two tragic examples of the effects of long-continued arsenical medication. The first concerns a man who had been taking Fowler's solution in huge doses—up to 1 dr. thrice daily—for every attack of the severe dermatitis herpetiformis for which he had been invalided from the Army after the last war. Needless to say no doctor had ordered the drug in such quantities, and he was unwilling to disclose the source of his supplies. I lost sight of him for some years and was eventually approached by his widow's solicitors who claimed compensation from the Ministry of Pensions on the score that the bronchial carcinoma from which he had died was caused by the arsenic which he had taken to relieve his compensable Duhring's disease. As there had never been a similar case recorded, and there was no evidence that the skin had been simultaneously affected the widow lost her appeal. The other patient had taken arsenic—uncontrolled for fourteen years—for psoriasis and came under my care for ulceration which had apparently developed in arsenical keratoses on the dorsum of his left foot. This was proved to be carcinomatous of squamous type and the foot was amputated. The disease recurred in the stump some months later and a thigh amputation was performed. Death ensued later from secondary deposits and cachexia. Is it possible in these days for patients to obtain repeats of arsenical prescriptions from the dispenser without further medical intervention?

POSTSCRIPT.—Inquiry has elicited the disturbing information that there is still no legal liability attached to such uncontrolled repetition.

The President: A patient cannot get arsenic without a prescription but with a prescription an arsenical mixture can be repeated *ad infinitum*.

Dr. Brian F. Russell: In these cases the dispenser had written out the prescriptions in full, periodically, to remind the prescribers and to save reference back through many pages of "Rep. Mist".

Dr. I. Muende: I was particularly interested in the case which had been reported as developing squamous-celled carcinomata, and was not convinced from the section that the lesions were of that nature. The tumour suggests a *nævo-carcinoma*, the epidermis being normal in parts, and beneath this there were *nævus* cells and deeper, a malignant proliferation of these cells.

The President: My view is that seborrhœic warts do not go on to epithelioma and that those on the forehead which are said to have turned into squamous epitheliomata were really senile keratoses, not seborrhœic warts at all. It would be interesting to know what the experience of the Section as a whole has been.

Dr. W. N. Goldsmith: I do not think I have ever seen this happen. But these patients have seborrhœic warts and it is interesting in view of Dr. Muende's opinion as to the histology of one of the cancers. The development of multiple carcinomas at the age at which they do appear in these patients reminds one of the efflorescent seborrhœic warts. They may depend upon developmental anomalies just as epitheliomas on the face and scalp often do.

Dr. W. Freudenthal: There are only a few well-investigated cases on record in which a seborrhœic wart has become malignant (e.g. Sibley and Muende, *Proc. Roy. Soc. Med.*, 1932, 25, 670 and 926; H. P. Pinkus, *Arch. Derm. Syph.*, Berlin, 1933, 169, 58). I share the opinion of those who consider the seborrhœic wart not as a variety of the infective wart, but as a late-developing verrucous *nævus* (*nævus tardus*). It is not surprising that this *nævus* sometimes, though very rarely, undergoes a malignant change. After all, practically any skin lesion, even a scar, might turn malignant. It is certainly wrong, as some textbooks do, to look upon the seborrhœic wart as a precancerous condition.

The President: I find it difficult to regard a seborrhœic wart as a *nævoid* condition. Why should they appear in enormous numbers and always in old and not in young people?

Dr. I. Muende: The nature of seborrhœic warts is very puzzling, for, although there is much to support the view that they are late *nævoid* in origin, the fact that they develop in lines of scratch, seem to point to their having a virus *ætiology*.

Dr. W. Freudenthal: There was an elderly woman at Jadassohn's clinic with hundreds of seborrhœic warts, on whom for several years we tried to produce more lesions by all kinds of inoculation and irritation, but we failed. She never developed more warts at the places we irritated. There are many successful inoculations of ordinary warts

recorded, but to my knowledge no one has ever succeeded in inoculating a seborrhœic wart.

Dr. G. B. Dowling: The symmetrical distribution of these seborrhœic warts on the trunk and their tendency to follow lines of cleavage, seem to exclude infection as the cause.

Dr. W. N. Goldsmith: Often accompanying an outburst of seborrhœic warts women, at any rate, get little tags on the sides of the neck. In one case we took out a number of lesions to see if we could trace any connexion between the two. Some of the tags had a cellular nævus type of structure.

Dr. R. Klaber: I believe these mollusca fibrosa are essentially of the same nature as seborrhœic warts. I have seen the spontaneous disappearance of both types of lesion. I did not think at first it could be possible; but the tags on the neck or the seborrhœic warts can certainly vanish without treatment. That may be the real explanation of the note in a recent American paper in which it was suggested that the disappearance of seborrhœic warts resulted from taking testosterone, given for another condition (Garb, J., and Wise F., *Arch. Derm. Syph.*, Chicago, 1943, 48, 359). I have tried it myself since, at the suggestion of Dr. Barber, but have failed to note any response.

The President: H. J. Templeton (*Arch. Derm. Syph.*, Chicago, 1936, 33, 495) wrote an article on "Cutaneous Tags of Neck" some years ago. The writer decided that they definitely were not ordinary warts, whatever else they were.

Dr. G. B. Dowling: The tags and seborrhœic warts occur on the same people and they are people who have nævi of various kinds, especially freckles, moles and milium bodies.

Dr. R. Klaber: Is it not possible that all these cases represent a "forme fruste" of von Recklinghausen's disease?

Dr. Louis Forman: I have recently seen von Recklinghausen's disease with tumours and café au lait spots on a man who said they appeared suddenly at the age of 20. He also presented around the neck, small soft, pedunculated tumours, some skin-coloured and some brown-coloured.

Clinical Section

President—J. D. ROLLESTON, M.D.

[November 10, 1944, continued]



FIG. 1.—Preoperative X-ray showing position of growth.

Oesophagectomy.—A. DICKSON WRIGHT, M.S.

J. S., male, aged 59, gas worker.

Admitted 2.9.44, complaining of regurgitation of solid food for previous six weeks immediately after swallowing, accompanied by a sense of obstruction and low retrosternal pain. Liquid swallowed and returned. He had been living on fluids for 3 weeks.

On examination.—Although then in good general health barium swallow showed neoplastic obstruction in mid-oesophageal region (fig. 1).

4.9.44: Oesophagoscopy showed ulcerated growth. Biopsy taken. Bougies passed. Patient was put on good mixed, nourishing diet with vitamin extracts.

7.9.44: Oesophagectomy under cyclopropane (Dr. L. H. Morris) through 7th left intercostal incision. The growth $1\frac{1}{2}$ in. long was just below the aortic arch. The oesophagus was mobilized by digital dissection and then the diaphragm incised, stomach mobilized by ligature of left gastric artery and vasa brevia and delivered through it. The cardiac end of stomach and small group of cardiac glands were removed with oesophagus and growth. The stomach was then brought up to meet the oesophagus below aortic arch and sutured with interrupted silk sutures; the mucous membranes were sutured with catgut. The site of the anastomosis was dusted with penicillin and sulphona-mide powder and the patient also received systemic penicillin for three days post-operatively.

Recovery was smooth with normal swallowing from twelve hours after operation.



FIG. 2.—The site of anastomosis shown level with aortic arch.



FIG. 3.—Large filling defect in stomach produced by heart.

2.10.44: On discharge he was able to swallow all solid foods. He was well and gaining weight (figs. 2 and 3).

Pathological report: Highly keratinized squamous-celled carcinoma. Growth found in all cardiac glands examined.

[December 8, 1944]

MEETING HELD AT MIDDLESEX HOSPITAL, LONDON, W.1

Spina Bifida Occulta.—P. H. SANDIFER, M.R.C.P.

Miss K. H., aged 27.

History.—Reported to hospital November 1944 complaining of winter "chilblains" of the dorsum of the left foot and toes. In the summer the left foot is cold, swollen and red, but in the winter it is dusker and painful. Her mother stated the trouble dated from birth and that the legs were normal save for "chilblains" till she was 5. She says her feet do not sweat even in hot weather. She admits not being able to run or jump like other people since puberty. She has walked with a slight limp for years, the left leg somehow not working as well as the right. She denies any sphincter disturbance, but occasionally she has to void urine at night. There is no pain, tingling or numbness save in the left foot when it is cold. It is absent when she is warm. Her symptoms are non-progressive. **Family and past history.**—Nothing relevant.

On examination.—Muscle tone slightly increased both legs. Wasting left thigh and calf respectively $\frac{3}{4}$ and 1 in. less in circumference than the right. Some pes cavus more marked left than right. Slight reduction of power at left ankle and toe joints though she can move them strongly against considerable resistance. Reflexes: All tendon-jerks exaggerated in the legs though the knee-jerk is less brisk in the left than the right. The left plantar response is extensor. The abdominal reflexes are brisk and equal. Sensation: Pin-prick, touch and temperature are not so well felt in the coldest areas of the left foot (dorsum and toes). Joint position is appreciated in all the toes. Vibration not so well perceived over the bony points of the left foot. The left foot is cold, dry, and red with blue mottled areas particularly in the toes. The nails are opaque and brittle. The right foot is cold. Pulsation of the dorsalis pedis and posterior tibial arteries less marked on the left. Over the lumbar spine a bone defect can be easily felt and below this there is a well-developed mop of hair. X-rays show spina bifida of L.V.3, 4, and 5 and S.1.

Comment.—The case is unusual because it is the vasomotor disorder which brings her to hospital; there is no evidence of gross cauda equina involvement and the sphincters are spared: finally the part of the nervous system which has suffered most is the cord.

Idiopathic Steatorrhœa: Osteomalacia.—J. E. G. PEARSON, D.M.

E. T., female, aged 39.

History.—A healthy child, always small. 1933: Normal pregnancy and parturition; baby well. Anæmia with sore tongue at this time diagnosed as pernicious anæmia. Treated with liver injections. 1938: Colitis. 1941: Present symptoms started with dragging of right leg, cramps in legs, and coldness and swelling of ankles. Has not walked for three years; almost bedridden.

Family history.—Not significant. **Past history.**—Patient has had pale and rather loose stools off and on for many years. Suggestion of some skeletal deformity since childhood.

Examination on admission (1.4.44).—Intelligent and co-operative patient. General condition: Thin. Growth stunted: Skeleton deformed, particularly pelvis, spine and thorax. Hip movements almost completely inhibited by severe pain. Muscle wasting. Slight genu valgum. Slight clubbing of fingers. Slight anæmia. No glossitis. Signs of latent tetany (Chvostek and Trousseau positive).

Investigations.—X-ray: Rarefied areas in skull. Widespread decalcification with deformity in thorax, spine and pelvis. No metastatic calcification seen in abdomen.

Blood-count.—Hb. 84%; R.B.C. 4,100,000; C.I. 1.0. M.C. diameter 7.9 μ . Blood calcium 8.0 mg.%. Alkaline phosphatase 140 units/100 c.c. Blood phosphates 1.2 mg.%. Faecal fats: Neutral 3.7%; soaps 37.6%; free fatty acid 22.7%. Total = 64%. Plasma proteins 7.25 g.%.
Treatment.—Physiotherapy for legs and spine. Fat-free diet. Skimmed milk: 2 pints daily. Liver extract intramuscularly in decreasing dosage. Vitamins, ultraviolet rays. Ferrous sulphate. Calcium gluconate 10 c.c. intravenously for one week daily; 10 c.c. intramuscularly alternate days for four weeks and gr. 20 q.i.d. Now gr. 20 t.d.s.

Further investigations.—19.5.44: Alk. phosphatase 100 units; phosphates 2.0 mg.%; calcium 9.6%. 24.5.44: Faecal fats: Neutral 1.9%; soaps 14.4%; free fatty acid 22.7%. Total = 39%. Serial X-rays show marked increase in bone calcification of pelvis and skull. November 1944: Alkaline phosphatase 70 units/100 c.c.

Course.—In four weeks after onset of treatment, legs could be moved freely without pain. In seven weeks, sitting out of bed in chair. In nine weeks started walking with stick and now walking well.

Massive Renal Calculi. Squamous-Cell Carcinoma in Lung, ? Primary. ? Secondary to Growth in Renal Pelvis.—J. E. G. PEARSON, D.M.

S. L., male, aged 60.

History.—Loss of strength. Loss of one stone in weight in the past two years. Pain in left side of abdomen, never sharp, worse after food. Increasing flatulence. Slight cough and dyspnoea. No sputum. Some burning on micturition—no frequency.

On examination.—Pale, slightly anæmic. Chest: Impaired percussion note, weaker breath sounds and pleural rub, right upper zone anteriorly. Abdomen: Large, hard irregular mass on left side, extending into the loin, partly movable. Prostate normal.

Investigations.—*Blood-count:* Hb. 86%; W.B.C. 6,000; neutros. 74%. X-ray of chest: Well-defined rounded shadow in right upper lobe peripherally.

Intravenous pyelogram: Right kidney normal; left kidney no secretion, numerous massive calculi. Barium enema: No filling defect in colon. Casoni test negative.



FIG. 1.—X-ray of chest showing well-defined rounded shadow in right upper lobe peripherally.



FIG. 2.—Intravenous pyelogram: Renal calculi left kidney, no secretion; normal secretion right kidney.

Urine: Sp. Gr. 1020. Acid. Albumin present. Blood absent. Pus cells profuse.

Punch biopsy of pulmonary lesion—second space anteriorly—shows histology of structureless material, blood clot and numerous fragments of well-differentiated squamous carcinoma. Blood urea 26 mg.%. It is considered that the pulmonary lesion is a primary neoplasm, and a thoracic surgeon is to be consulted about the possibility of pneumonectomy.

Carcinoma of the Trachea.—K. P. BALL, M.D. (for R. A. YOUNG, C.B.E., M.D.).

W. B., male, aged 46. Bus driver.

History.—Admitted on 15.11.44. He complained of a non-productive, paroxysmal cough since August 1944. He had had three small hæmoptyses and had noticed a pain over his right shoulder with swelling above his right clavicle since October 1944. Shortly before admission he had lost his voice. *Past history.*—Not significant.

On examination.—There was a firm, fixed mass of glands beneath the origin of the right sternomastoid, displacing the trachea to the left, but apparently separate from it. There were scattered sonorous rhonchi throughout the chest. Laryngoscopy revealed complete paralysis of the right vocal cord. X-ray of chest showed enlargement of the right paratracheal glands. Tomography showed a mass encroaching on the lumen of the trachea from the right, about 1 in. above the bifurcation. Bronchoscopy: An ulcerated swelling was seen on the right posterolateral wall of the lower part of the trachea, causing considerable narrowing. A biopsy was taken and histology showed invasion of the tissues by relatively undifferentiated squamous-celled carcinoma: small areas of spine cell formation were present, but no keratinization. He has had much wheezing and difficulty in coughing up blood-stained sputum. A further X-ray shows that he has

developed consolidation of the lingular process of the left lung. He is having deep X-ray therapy.

Plummer-Vinson Syndrome with a Post-Cricoid Web.—K. P. BALL, M.D. (for G. E. BEAUMONT, M.D.).

Mrs. L. C., aged 52. Housewife. *History.*—First attended on 3.6.44. She complained of a sore mouth, difficulty in swallowing, shortness of breath and tiredness. Her symptoms had been increasing for two years. Her periods were still moderately heavy. Her diet consisted of bread and butter or cake, and tea for all meals except for lunch, when she had gravy and vegetables. She never ate meat. On examination. — Mucosæ pale. Cracks at corners of mouth, and a small ulcer inside the lower lip. Tongue pale with atrophic mucosa. Marked koilonychia present. Tip of spleen palpable. *Blood-count.* — Hb. 45%; R.B.C. 4,600,000; C.I. 0.5; W.B.C. 5,000. Barium swallow showed a post-cricoid web at the level of C.5 (see fig.).



X-ray of barium swallow, showing a post-cricoid web at the level of C.5.

She was treated with pil. ferri sulph. gr. 6 t.d.s., and she rapidly improved. On 29.8.44 her Hb. was 99% with C.I. 0.98. The stomatitis and koilonychia disappeared, but the improvement in her swallowing was less marked. On 8.12.44 a further barium swallow showed that the web was still present, and did not appear to have altered, in spite of the diminished dysphagia.

Rheumatoid Arthritis with Subcutaneous Nodules.—K. P. BALL, M.D. (for G. E. BEAUMONT, M.D.).

Mrs. L. S., aged 44. Shop assistant.

History.—Admitted to hospital on 23.10.44. She had had an insidious onset of arthritis with pain and stiffness in the right thumb in 1931. This spread to both hands, elbows and ankles. She then improved with no particular treatment and remained well until 1940. Since then the condition has steadily progressed, especially during the past six months. In June 1944 she noticed the subcutaneous nodules for the first time.

Past history.—Not relevant. No rheumatic fever or chorea.

On examination.—Typical deformity of rheumatoid arthritis affecting hands, elbows, shoulders, knees and ankles. Considerable pain and stiffness in the back. Subcutaneous nodules present over occiput, olecranon and acromion processes, and over both patellæ. They vary in size from a split-pea to a small cherry, those over the acromion processes being the largest. The right epitrochlear and both sets of axillary lymphatic glands are considerably enlarged, and there are small glands in both posterior triangles. Spleen not palpable. B.P. 100/80. No abnormality in the heart.

Investigations.—X-ray of the hands shows marked atrophic arthritis, with destruction and partial ankylosis of the carpal joints. Sedimentation rate, 65 mm. in one hour (Westergren). Blood uric acid 2.9 mg. per 100 c.c. Histology of nodule removed from over right patella: "The nodule consists of fibrous tissue in which are small areas of necrosis, each surrounded by a small zone of radiating endothelial cells and a sparse infiltrate of polymorphonuclear leucocytes, lymphocytes and plasma cells."

Dr. F. Parkes Weber said that the subcutaneous nodules in this case were excellent examples of what he proposed (*Lancet*, 1944 (ii), 611; and *Ann. Rheum. Dis.*, 1944, 4, 3) to call "chronic necrobiotic nodules of the rheumatoid arthritis type"—in order to distinguish them from rarer types of nodules occasionally present in rheumatoid arthritis cases. Dr. Ball's patient likewise showed the characteristic painless lymphadenopathy of the active periods of rheumatoid arthritis, which might disappear when the joint symptoms became quiescent. Such enlarged lymphatic glands on microscopic examination presented the picture of a non-specific follicular lymphadenopathy with large "germ-centres" of Flemming. These germ-centres likewise constituted a microscopic feature of the affected synovial membranes in rheumatoid arthritis. A painless superficial lymphadenopathy was much more frequent in advanced rheumatoid arthritis cases than was commonly supposed. The patients were usually quite unaware of it. It was of course a constant feature of "Still's disease", which Dr. Weber regarded as only a variety of rheumatoid arthritis.]

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[November 24, 1944]

Smallpox and Vaccination in British India During the Last Seventy Years

By Sir LEONARD ROGERS, K.C.S.I., M.D., F.R.C.P., F.R.S., I.M.S., Ret.

INDIA is the largest and most populated area of the world in which the virulent type of smallpox is endemic. From it, infection is frequently brought by sea to Great Britain and other countries, as in the Glasgow outbreak of 1942. Statistics of smallpox mortality are available for British India (but not for the Native States) from 1868, together with vaccination returns since 1877. In 1909 the statistical officer to the Government of India, Major (now Lieut.-Colonel) S. P. James, F.R.S., I.M.S., demonstrated by a study of the data, illustrated by diagrams showing the yearly smallpox death-rates per mille and the number of vaccinations, that a great decline in smallpox had coincided with a great increase of vaccinations in the absence of improved sanitation or other possible cause of the decline other than vaccination. In 1925 Rogers brought the records up to 1921 and showed that both the fall in smallpox deaths and the rise in vaccinations had continued. As statistics for an additional eighteen years are now available a further study of the subject may be of value.

Handicaps to vaccination in India.—It has recently been stated by Dr. K. Millard that attempts to control smallpox in India by universal vaccination had signally failed. The difficulties in carrying out such a measure among the 380 million people of India, some 90% of whom reside in about one million villages, scarcely any of which have a doctor, therefore require mention. In a recent report the Director of Public Health for India wrote: "Defective registration of births renders it possible for large numbers of children to escape vaccination, even in areas where a compulsory vaccination act is in force: vaccination continues to be optional over large tracts of the country and, even in compulsory areas, the law is enforced by the local authorities in only a perfunctory manner." As a matter of fact as late as 1909 James recorded that vaccination was only compulsory in 7% of British India; yet a great decline in smallpox had already been achieved by voluntary measures: even in 1937 under half the population were subject to compulsory vaccination. The above report goes on to record that: "No public health department is sufficiently manned to enable it suitably to deal with the whole population under its control and, until this is done it will be impossible to ensure that smallpox disappears from the list of epidemic diseases from which India continues to suffer." Although India is thus very far from having established universal vaccination, nevertheless the Director of Public Health has recently recorded his opinion regarding the use of vaccination in India thus: "As a result of the encouraging work carried on within recent years a large amount of unnecessary sickness, suffering and disablement has been prevented; with further efforts there is every hope that greater benefits will accrue." The following data will suffice to endorse that conclusion.

Earlier smallpox incidence in India.—Temples all over India dedicated to the goddess of smallpox testify to the ravages of the disease for thousands of years past. As late as 1849 nearly 13% of all the Calcutta deaths were due to smallpox; much the same rate as the 12% of London smallpox deaths in prevaccination days of the eighteenth century. As late as 1869, when vaccination departments had only very recently been organized in all the provinces of India, it is on record that 95% of the population had suffered from smallpox at some period of their lives. Earlier in the nineteenth century Ranald Martin reported that 75% of blindness in India was due to smallpox; in 1909 recorded census figures showed a reduction in blindness in India during the two decades 1881 to 1901 of 44% coincidentally with a great decline in smallpox and increase of vaccinations. James reported many instances between 1869 and 1879 of smallpox death-rates both of towns and of whole districts, commonly with over one million inhabitants, of from 10 to 32 per mille in a single year.

developed consolidation of the lingular process of the left lung. He is having deep X-ray therapy.

Plummer-Vinson Syndrome with a Post-Cricoid Web.—K. P. BALL, M.D. (for G. E. BEAUMONT, M.D.).

Mrs. L. C., aged 52. Housewife. *History.*—First attended on 3.6.44. She complained of a sore mouth, difficulty in swallowing, shortness of breath and tiredness. Her symptoms had been increasing for two years. Her periods were still moderately heavy. Her diet consisted of bread and butter or cake, and tea for all meals except for lunch, when she had gravy and vegetables. She never ate meat. *On examination.*—Mucosæ pale. Cracks at corners of mouth, and a small ulcer inside the lower lip. Tongue pale with atrophic mucosa. Marked koilonychia present. Tip of spleen palpable. *Blood-count.*—Hb.



X-ray of barium swallow, showing a post-cricoid web at the level of C5.

45%; R.B.C. 4,600,000; C.I. 0.5; W.B.C. 5,000. Barium swallow showed a post-cricoid web at the level of C5 (see fig.).

She was treated with pil. ferri sulph. gr. 6 t.d.s., and she rapidly improved. On 29.8.44 her Hb. was 99% with C.I. 0.98. The stomatitis and koilonychia disappeared, but the improvement in her swallowing was less marked. On 8.12.44 a further barium swallow showed that the web was still present, and did not appear to have altered, in spite of the diminished dysphagia.

Rheumatoid Arthritis with Subcutaneous Nodules.—K. P. BALL, M.D. (for G. E. BEAUMONT, M.D.).

Mrs. L. S., aged 44. Shop assistant.

History.—Admitted to hospital on 23.10.44. She had had an insidious onset of arthritis with pain and stiffness in the right thumb in 1931. This spread to both hands, elbows and ankles. She then improved with no particular treatment and remained well until 1940. Since then the condition has steadily progressed, especially during the past six months. In June 1944 she noticed the subcutaneous nodules for the first time.

Past history.—Not relevant. No rheumatic fever or chorea.

On examination.—Typical deformity of rheumatoid arthritis affecting hands, elbows, shoulders, knees and ankles. Considerable pain and stiffness in the back. Subcutaneous nodules present over occiput, olecranon and acromion processes, and over both patellæ. They vary in size from a split-pea to a small cherry, those over the acromion processes being the largest. The right epitrochlear and both sets of axillary lymphatic glands are considerably enlarged, and there are small glands in both posterior triangles. Spleen not palpable. B.P. 100/80. No abnormality in the heart.

Investigations.—X-ray of the hands shows marked atrophic arthritis, with destruction and partial ankylosis of the carpal joints. Sedimentation rate, 65 mm. in one hour (Westergren). Blood uric acid 2.9 mg. per 100 c.c. Histology of nodule removed from over right patella: "The nodule consists of fibrous tissue in which are small areas of necrosis, each surrounded by a small zone of radiating endothelial cells and a sparse infiltrate of polymorphonuclear leucocytes, lymphocytes and plasma cells."

Dr. F. Parkes Weber said that the subcutaneous nodules in this case were excellent examples of what he proposed (*Lancet*, 1944 (ii), 611; and *Ann. Rheum. Dis.*, 1944, 4, 3) to call "chronic necrobiotic nodules of the rheumatoid arthritis type"—in order to distinguish them from rarer types of nodules occasionally present in rheumatoid arthritis cases. Dr. Ball's patient likewise showed the characteristic painless lymphadenopathy of the active periods of rheumatoid arthritis, which might disappear when the joint symptoms became quiescent. Such enlarged lymphatic glands on microscopic examination presented the picture of a non-specific follicular lymphadenopathy with large "germ-centres" of Flemming. These germ-centres likewise constituted a microscopic feature of the affected synovial membranes in rheumatoid arthritis. A painless superficial lymphadenopathy was much more frequent in advanced rheumatoid arthritis cases than was commonly supposed. The patients were usually quite unaware of it. [It was of course a constant feature of "Still's disease", which Dr. Weber regarded as only a variety of rheumatoid arthritis.]

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

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Handicaps to vaccination in India.—It has recently been stated by Dr. K. Millard that attempts to control smallpox in India by universal vaccination had signally failed. The difficulties in carrying out such a measure among the 380 million people of India, some 90% of whom reside in about one million villages, scarcely any of which have a doctor, therefore require mention. In a recent report the Director of Public Health for India wrote: "Defective registration of births renders it possible for large numbers of children to escape vaccination, even in areas where a compulsory vaccination act is in force: vaccination continues to be optional over large tracts of the country and, even in compulsory areas, the law is enforced by the local authorities in only a perfunctory manner." As a matter of fact as late as 1909 James recorded that vaccination was only compulsory in 7% of British India; yet a great decline in smallpox had already been achieved by voluntary measures: even in 1937 under half the population were subject to compulsory vaccination. The above report goes on to record that: "No public health department is sufficiently manned to enable it suitably to deal with the whole population under its control and, until this is done it will be impossible to ensure that smallpox disappears from the list of epidemic diseases from which India continues to suffer." Although India is thus very far from having established universal vaccination, nevertheless the Director of Public Health has recently recorded his opinion regarding the use of vaccination in India thus: "As a result of the encouraging work carried on within recent years a large amount of unnecessary sickness, suffering and disablement has been prevented; with further efforts there is every hope that greater benefits will accrue." The following data will suffice to endorse that conclusion.

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Vaccination in India.—Inoculation of smallpox virus had for long been used in some parts of India and often spread the infection. It was not until 1870 that its use was condemned by the Government of India but it proved very difficult to suppress. An active vaccine lymph first reached India in 1802 but it was not until 1827 that Bombay organized systematic vaccination with European supervisors over native vaccinators. This province for long was far ahead of other parts of India with the result that in the first decade of smallpox mortality statistics Bombay had a considerably lower incidence than any other province. The Bombay system was extended to the United Provinces in 1854, but it was only between 1864 and 1868 that it was extended to other provinces. Thus when smallpox mortality figures first became available in 1868 for British India, vaccination departments had only very recently been organized on a large scale, so its effects can be judged.

The reduction of smallpox incidence in India coincidently with the increase of vaccination.—We may now turn to the data in Table I of the smallpox incidence and vaccinations in the seven decades 1868-77 to 1928-37, and the chart showing the yearly rates per mille and the millions of vaccinations annually for the whole period. It has long been recognized that increased or epidemic prevalence of smallpox occurs in India about every five to seven years; this is partly attributable to the accumulation of susceptible unvaccinated children in the intervals between the outbreaks: it is well illustrated by the chart of the annual rates per mille. These exacerbations are smoothed out in the ten-yearly data in Table I which demonstrates at a glance the steady decline in the average rates per mille in column 2 coincidently with the rise in the average annual millions of vaccinations, so the chart requires little explanation.

TABLE I.—SMALLPOX INCIDENCE AND VACCINATION IN BRITISH INDIA IN SEVEN DECADES

Years	Smallpox, total deaths	Average rates per mille	Population in millions	Average yearly millions of vaccinations
1868-77	1,436,890	1.032	142,000,000	?
1878-87	1,460,890	0.772	190,000,000	4.75 millions
1888-97	961,424	0.466	206,000,000	6.75 "
1898-1907	832,165	0.374	222,000,000	8.75 "
1908-17	851,099	0.364	234,000,000	9.50 "
1918-27	832,477	0.347	240,000,000	14.50 "
1928-37	763,279	0.290	263,000,000	19.1 "

Owing to the increase in each decade in the population on which the rates per mille are calculated, the total deaths in each decade shown in column 2 are not comparable, as are the rates per mille in column 3. The population dealt with in 1878-87 was no less than 33% greater than in the previous decade: hence the large fall in the rate per mille in 1878-87 in spite of a small increase in the actual smallpox deaths in that decade.

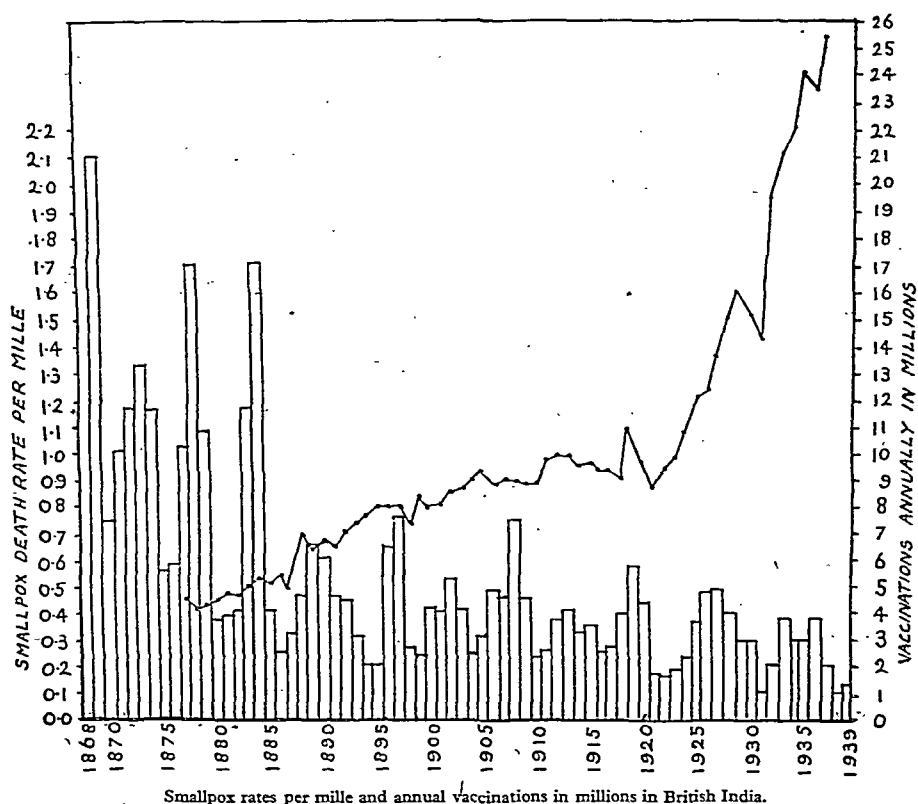
It will be observed that the average smallpox death-rate per mille in the last decade of 1928-37 was three and a half times less than that of 1868-77. Moreover the most rapid decline in the smallpox death-rate from 1.032 in 1868-77 to 0.374 in 1898-1907 coincided with the most rapid increase up to that time in the average yearly vaccinations from a small, but not precisely known, number in the first decade to 8,750,000 in 1898-1907. The last decade showed the next largest decline of smallpox incidence when the vaccinations rose from 14.5 to 19.1 millions, mainly due to more revaccinations during outbreaks of smallpox. It is too early to see the full effects of that increase. On the other hand, the smaller, but steady declines of smallpox incidence in the intermediate decades occurred at the time when the decennial average increases in the number of vaccinations were comparatively small; due largely to the handicap of the recent plague pandemic being then at its height. There is thus a close relationship between the increased number of vaccinations and the decline of smallpox throughout the whole seventy years.

Decline in the severity of smallpox epidemics with increased vaccination.—This is evident from a glance at the chart; it is illustrated by Table II.

TABLE II.—SMALLPOX DEATHS PER MILLE IN EPIDEMIC YEARS.

Years	1869	1873	1878	1884	1889	1897	1908	1919	1927	1933-36
Deaths per mille	2.1	1.32	1.68	1.70	0.63	0.77	0.75	0.56	0.49	0.38
Rainfall deficient in	?	?	1877	1883	1888	1896	1907	1918	1926	1932

It will be observed that the height of the 1933-36 exacerbation was five and half times less than that of 1869, in accordance with the fourfold increase in the yearly vaccination in 1928-37 decade as compared with those of 1878-87 and a still greater but unknown rise over those of 1868-77. Here again the greatest decline in the severity of the epidemics occurred during the second to fourth decades of the greatest proportional rise in the number of vaccinations. They have also become less frequent with longer intervals between them in recent years.



As I showed in 1926 the degree of increased mortality in any particular epidemic is largely dependent on low rainfall in the south-west monsoon period from June to September of the previous year which prevents a seasonal rise in absolute humidity high enough to reduce the minimum yearly smallpox incidence at the end of the monsoon to its usual low level. The annual cold weather rise thus starts from a higher level and reaches epidemic levels. Thus the three highest smallpox exacerbations of the last three decades each followed previous low monsoon rains; yet even in such unfavourable years the smallpox outbreaks remained at several times lower levels than those of the first two decades of very deficient vaccination as shown in the chart; yet another striking piece of evidence of the value of vaccination in controlling smallpox epidemics in India in recent decades.

Smallpox epidemics in well-vaccinated and poorly vaccinated provinces respectively.—This aspect of the question was dealt with by James in 1909 when he demonstrated that in the six well-vaccinated provinces of India ten major smallpox epidemics during 1868 to 1887 were reduced to none during 1888 to 1907; yet in the three poorly vaccinated provinces of North-East India and Lower Burma during the same periods the major epidemics were only reduced from seven to five. There is thus a direct relationship between the efficiency of vaccination in different provinces of India and the elimination of serious epidemics of smallpox.

Smallpox incidence in adjacent well- and poorly vaccinated areas respectively.—James also pointed out that in India it is easy to compare the incidence of smallpox in adjacent areas with precisely similar conditions, except as regards the efficiency of vaccination, of which the following example will suffice: In the decade 1893-1902 the smallpox annual death-rate per mille in an Orissa State, with very little vaccination (only 4 per mille) was 15.0; in the adjacent British province the smallpox rate in the same decade was 0.4, 37½ times less! As late as 1938 high smallpox death-rates were noted in Native States.

In summarizing his conclusions from such comparative data Colonel James pointed out that the records proved that inquiries in from 60 million people down to a few hundreds

"the result is invariably the same—well-vaccinated areas show a remarkable decline in smallpox while non-vaccinated or badly vaccinated areas show no such decline"

Improved sanitation cannot account for the reduction of smallpox mortality in India.—James also discussed fully every cause, other than vaccination, that has been suggested to account for the decline of smallpox in India; he concluded that "there is no other cause that will account satisfactorily for the facts". The only other suggested cause that need be considered here is the frequent statement of opponents of vaccination that improved sanitation is the essential factor that has led to the diminution of smallpox in various countries. The following facts disprove that assertion as regards India:

(1) During the decades when smallpox so greatly declined in India there has been but little improvement in sanitation, except improved water supplies in the larger cities and towns; and none at all in the million or so villages in which nearly 90% of the population live.

(2) As was pointed out by James, cholera is far more easily controlled by sanitary measures than smallpox; yet he demonstrated by a chart of the yearly cholera rates per mille of British India from 1875 to 1907, during which the main decline in smallpox incidence took place in India, there was no diminution in the cholera incidence.

(3) In the case of a disease that is so readily communicated by contagion or possibly by aerial infection as smallpox, the most important sanitary condition that can well bring about a material decline in its incidence is a marked decrease of overcrowding. Yet the 85% increase in the population during the last six decades has much increased overcrowding in towns and in the villages. Moreover, in the same period, greatly increased facilities of travel by road and rail, and recently by motor bus, have much increased the facilities for the spread of smallpox in India. The great decrease of the disease in India has therefore occurred in spite of sanitary and other conditions being such as might have been expected to have led to an increase rather than a decrease of the disease in this vast endemic area.

The saving in life due to vaccination in India.—The saving of life due to the reduction of smallpox deaths in India during the last six decades can be estimated by working out the number of deaths that would have occurred in each decade had the high rate per mille of 1868-77 been maintained among the increasing population of the six subsequent decades and subtracting from those figures the actual number of recorded deaths. The result shows a saving of 8,750,000 lives in the sixty years and an average yearly decrease of 200,000 deaths a year during the last decade of the series. The true saving in life is nearly twice that huge figure because it is on record that the returns of the first decade of 1868-77 were only about half the true figure. And this great control of the smallpox mortality has been obtained through vaccination mainly voluntary and never anything like universal. The measure has also been most severely handicapped until comparatively recently by the lack of anything like organized vaccination in the greater part of the intermingled 560 Native States, which occupy 39% of the area of India with a population of 80 million people.

CONCLUSIONS

(1) All the data of smallpox death-rates and the annual number of vaccinations since they became available for the seven decades up to 1939 (wartime figures are not obtainable) have been charted. They show that the smallpox death-rates per mille have declined in British India to three and a half times less than in the first decade of the series and the height of the periodical epidemics to five and a half times less; *pari passu* with an increase in the annual vaccinations from about two to nineteen millions. The decrease was greatest in the early years in the provinces in which vaccination was most efficient.

(2) At the period of the most rapid decline of smallpox in British-administered India the smallpox death-rates per mille in Indian States, with little or no vaccination, were anything up to 37 times as great as in adjacent fairly well-vaccinated British-administered districts.

(3) The great reduction in smallpox following a great increase in vaccinations cannot be due to improved sanitation because (a) there has been no material improvement in sanitation of the million or so villages in which about 90% of the population reside; (b) there has been no such great decrease in the mortality from cholera, although that disease is far more easily controlled by sanitary measures than is the highly contagious smallpox (James).

(4) If the high smallpox death-rate of the first decade had continued unabated among the rapidly increasing population upwards of eight million more deaths would have

urred during the last six decades than were recorded. This substantial degree of control of smallpox in India has been obtained very largely through voluntary vaccination, which has never been anything like universal, and under great difficulties in the most important endemic area in the world of the virulent type of smallpox. It constitutes one of the greatest benefits of British rule in India.

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Dr. C. Killick Millard said that the so-called vaccination question was really two questions, though they were often treated as one: (1) The effect of vaccination in protecting the individual; (2) the effect of vaccination in protecting the community.

Theoretically it was quite possible that whilst vaccination protected the individual—as he was quite satisfied it did—it might fail entirely to protect the community, or indeed it might even tend to increase the disease, a possibility which could not be entirely excluded. That vaccination temporarily protected the individual had been so abundantly proved that he had not hesitated to take his own wife and young children into the Leicester smallpox hospital where he had photographed them by the bedside of a bad confluent case.

But when it came to protecting the community the case was quite different. It would be feasible to protect a small "closed" community like the staff of a smallpox hospital even if the protection conferred by vaccination only lasted for six months; but it had never yet been found practicable similarly to protect the general population of a whole country. Infantile vaccination, however complete, was quite inadequate without repeated revaccination. It could no longer be held that it was vaccination of the community which had brought about the disappearance of smallpox from this country, because vaccination had declined *pari passu* with the decline in smallpox.

As regards India, Sir Leonard had shown a graph giving the smallpox mortality and the number of vaccinations during the past seventy years from which it was obvious that whilst smallpox mortality had decreased vaccinations had gone up, and in the last decade the increase had been very great. Sir Leonard contended that the whole of the decrease in the smallpox mortality was due to vaccination, but surely this was rather an optimistic assumption. The fall in mortality was very steep after the year 1884 with no corresponding increase in the amount of vaccination, which at that time must have been very incomplete. An alternative explanation, which seemed to him more probable, was that it was part of a similar decrease in smallpox mortality which occurred in many countries when the great pandemic of smallpox of the last quarter of last century passed away.

Sir Leonard had taken exception to a statement made by him (Dr. Millard) in a letter to the *Brit. med. J.*, 1942 (ii), 678, to the effect that India had signally failed in the attempt to control smallpox by vaccination, so that smallpox in India was still a terrible scourge. But could it really be denied that it had been a failure or that smallpox was still a scourge? According to Sir Leonard's own figures, during the last decade for which the figures were available (1928-37) there had been in British India no less than 763,000 deaths from smallpox, and that figure, appalling though it was, was almost certainly an under-statement, for in the Report of the Public Health Commissioner for 1936 reference was made to the very large number of deaths registered as due to chicken-pox which were doubtless really due to smallpox. Such a mortality in Great Britain with a population of 46 millions, would mean an average of over 13,000 deaths from smallpox each year. Such a result he thought would be regarded by most people as a very signal failure. Of course, the difficulties in India were infinitely greater, owing to the backwardness of the country and the characteristics of the people, but whilst this explained the failure it did not alter the fact that there had been a failure, and, he would even say, a tragic failure. That did not mean that vaccination had done no good, and if he had a friend going out to India he would strongly advise him to get vaccinated first.

Dr. M. N. Pai wished to emphasize three important aspects, i.e. the continued high incidence of smallpox and high mortality rate; the unsatisfactory state of vaccination; and the effect of these two factors on the health of the British and Allied troops.

In 1927 it was estimated that 50,000 persons had died of smallpox in the previous year. Ten years later this number had more than doubled itself and this increase cannot be explained wholly on the basis of increase in the population.

When the mortality in the Provinces is studied it is seen that the high incidence is confined chiefly to the N.W.F.P., the Punjab, Sind, Bengal and Assam and parts of Bombay, where the state of successful vaccination leaves much to be desired. Unfortunately these are the very provinces where a large number of British troops have been stationed. It is therefore worth knowing whether the health of the British troops has in any way been affected by the incidence of smallpox among the civilian population of these areas.

Even in such a select and highly protected community as the Army one finds that the incidence of smallpox among British troops and their families is higher in Northern and Eastern Commands than in the other Commands. As the territories covered by these two Commands correspond to the N.W.F.P., the Punjab, Bengal and Assam, the evidence for stating that the health of the civilian population has direct repercussions on the health of the military personnel appears convincing.

TABLE I.—INCIDENCE OF SMALLPOX IN INDIA 1939.

	British Provinces	Cases per 1,000
Indian Civilian	...	0.24
British N.C.O.s and Other Ranks	...	0.4
Wives of British N.C.O.s and Other Ranks	...	0.7
Children of British N.C.O.s and Other Ranks	...	0.2

Table I shows that a vaccinated and perhaps re-vaccinated British soldier in India has greater chances than (and the wife of a British soldier more than twice as many chances as) an Indian civilian of contracting smallpox. Therefore Britain cannot afford to ignore the medical and sanitary problems of India.

The main factors responsible for this unsatisfactory state include:

A. General.—(1) Inadequate provision for medical and public health measures: for a population of 388 millions there are only 42,000 doctors of whom only a few are qualified health officers. According to the Report of the Central Advisory Board of Health for 1939 "nearly one-half of the districts and three-quarters of the municipalities of British India are still without qualified health officers".

(2) "Every year large numbers of births escape registration and naturally these remain unvaccinated."

(3) "Notification of cases and deaths from smallpox leaves much to be desired."

(4) Cases of a mild type, so-called "alastrim", escape notification and it is not unusual for persons suffering from this type to travel by public vehicles and so spread the infection.

(5) Presence of Indian States where vaccination laws either do not exist or compulsory vaccination is prohibited.

B. Local.—(1) Vaccination is not compulsory in every province. To give only one instance, in the province of Sind out of a total of 37 sanitary committees only 7 have so far accepted the provisions of the Bombay Dist. Vaccination Act of 1892.

(2) In some provinces those successfully vaccinated have to pay a small sum. In a country where the level of average income is very low indeed this fee acts as a deterrent to vaccination.

Lastly, the greatest obstacle to the extension of vaccination and the reduction of mortality from smallpox has been the nation-wide campaign organized on behalf of the so-called Indigenous Systems of Medicine. Public funds which are badly needed for the extension of medical relief and sanitary measures are being frittered away in opening and maintaining Schools of "Indian Medicine" and in subsidizing practitioners who, in this or in any other civilized country, would be considered as no better than quacks.

No reduction in the incidence of smallpox or for the matter of that in any of the epidemic or endemic diseases is likely as long as India is dependent on the bondage of magic, mediocrity and mendicancy.

Sir Leonard Rogers, in replying to the discussion, said that the only criticism of his paper, that of Dr. Millard, is easily answered. Sir Leonard contended that Dr. Millard's published statement that attempts to "control" smallpox in India by universal vaccination had signally failed is inaccurate, misleading and unfair to the public health authorities of India. Dr. Millard refused to admit the validity of the work of Colonel James, I.M.S., who had had unique opportunities as Statistical Officer to the Government of India to adjudicate on the results of extension of organized vaccination to all the provinces of British-administered India during the two decades immediately preceding the great decline of smallpox in British India; although the epidemics continued unabated in unvaccinated areas of the hundreds of Native States, thus furnishing immense control areas. Nor will he admit the confirmatory evidence of fifty years of subsequent greatly reduced smallpox in the British-administered areas alone, with the saving of many million lives, as evidence of any material "control" of smallpox in India, although this has also been recently testified to by the Public Health Commissioner of India. In short, Dr. Millard, with experience solely in Great Britain (which is not an endemic area and in no way comparable to India) rejects *in toto* the seventy years' data and experience of all the most eminent public health authorities of India.

Dr. Millard attempts to evade the plain issue by pointing to the continued prevalence of smallpox in India, due to insuperable difficulties which Dr. Pai had confirmed: difficulties that only enhance the fivefold reduction in the height of the smallpox epidemics that has been obtained in British India. Yet Dr. Millard is unable to point to any other cause of the great reduction of smallpox that closely followed the general organization of vaccination in India, except a vague speculation on the decrease of the disease in distant countries with no relation to India. But the speaker has demonstrated that in India epidemic rises of smallpox always follow low previous rainfall and absolute humidity, and he has shown that such climatic conditions, extremely favourable to the severest smallpox epidemics in India, ceased throughout the last fifty years to produce such severe outbreaks as they did previously to the general adoption of vaccination throughout British India; yet such severe outbreaks continued in unvaccinated Native States, as Colonel James has demonstrated.

Dr. Millard has repeatedly asserted his strong belief that vaccination does protect against smallpox; at least when it is used according to his advice. Yet he confidently asserts that over 300 million vaccinations during recent decades had "signally failed" materially to "control" smallpox in India! Is this logical, to use his own phrase?

Nor is Dr. Millard consistent in his recent disparagement of the work of the public health authorities in India. In his book, "The Vaccination Question in the Light of Modern Experience" (published in 1914), he stated that the value of vaccination may be quite different in India and China "where the disease is endemic". "It is quite logical to suggest that it (vaccination) may be almost useless or even detrimental here (in Great Britain), although an incalculable boon there", that is in India and China.

PLATE I.



FIG. 1.

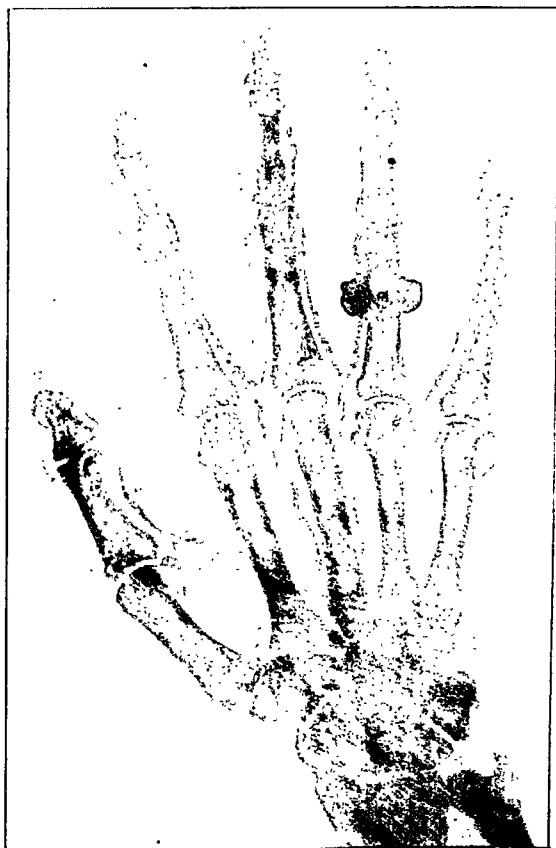


FIG. 2.

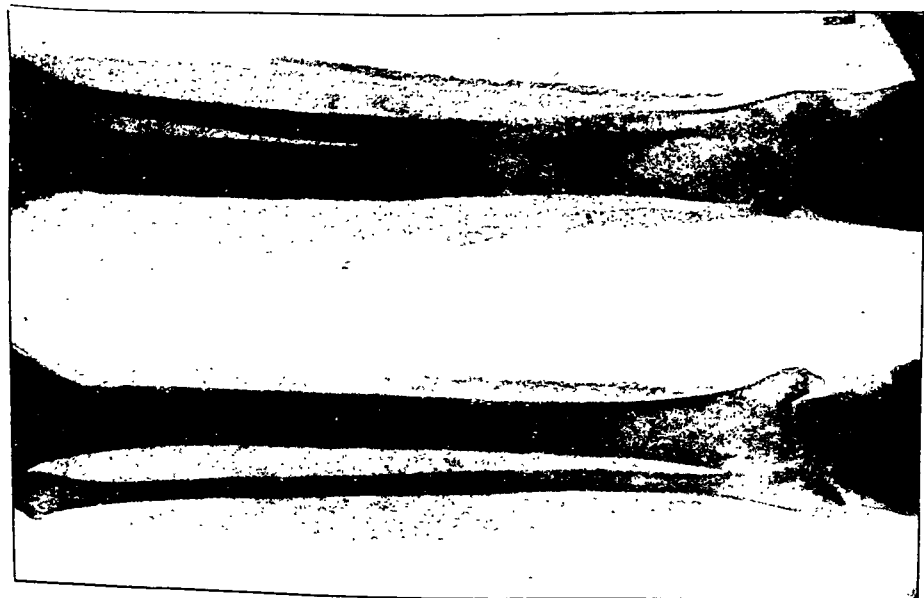


FIG. 3.

AGLEY, M.B., and DONALD HUNTER, M.D.: *Calcinosis in a Case of Nephritis with Secondary Hyperparathyroidism.*

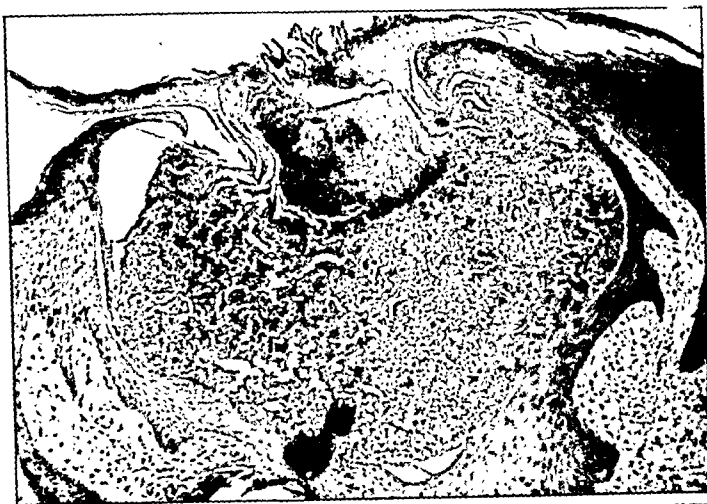


FIG. 4.

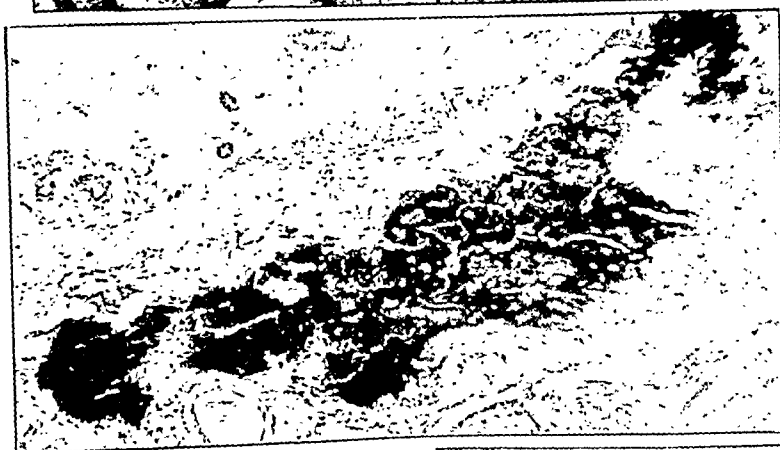


FIG. 5.



FIG. 6.

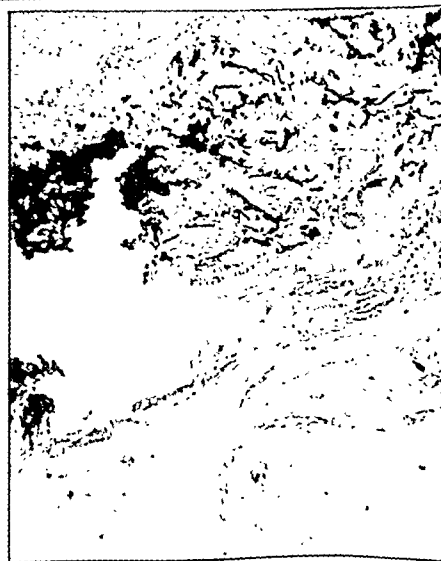


FIG. 7.

J. E. M. WIGLEY, M.B., and DONALD HUNTER, M.D.: Calcinosis in a Case of Chronic Nephritis with Secondary Hyperparathyroidism

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[November 16, 1944]

Calcinosis in a Case of Chronic Nephritis with Secondary Hyperparathyroidism.—J. E. M. WIGLEY, M.B., and DONALD HUNTER, M.D.

G. W., female, aged 21.

History.—Rupture of the left quadriceps tendon after a minor injury in 1942. Since then increasing pallor and loss of energy, some breathlessness, bulbous swellings on the ends of the fingers. August 1944: Appearance of an irritating skin condition in axillae and later over upper thighs, cubital fossae, groins, behind the knees, back of the neck, under the breasts and in the ano-genital region. The irritation has subsequently decreased.

October 1944: Amenorrhœa. Loss of 2 st. in weight during the past year.

Physical examination.—Very ill, apathetic and drowsy. Small and thin, but does not look emaciated. Pale skin and mucous membranes. Eruption in the areas mentioned consists of reddish-brown, isolated papules, linear lesions, and almost black indurated areas (fig. 1, axilla). Extending beyond these areas are many deep-seated flesh-coloured papules which feel like a layer of shot in the skin. The skin over these areas looks and feels dry and shiny, with slight scaling. There is no palpable thickening which might suggest scleroderma. Bulbous expansion of terminal phalanges with shortening of the nails but without swelling of the nailbed. Tenderness on squeezing the metacarpal heads, and of the sternum on percussion; pupils and fundi normal. Heart and lungs normal; blood-pressure 120/65 mm. mercury.

Urine: Sp. gr. 1006 (fixed); albumin present; Bence Jones protein absent; occasional pus cells; no sugar.

Blood.—R.B.C. 2,630,000 per c.mm. Hb. 46%; C.I. 0.86. W.B.C. 11,600 per c.mm.; 81.5% polys., 1.0% eosinos., 2.0% monos., 15.5% lymphos.

Serum calcium 9.8 mg.%; plasma phosphorus 3.4 mg.%; plasma phosphatase 17.2 units. Plasma proteins, total 6.7%; fibrin 0.6%, albumin 2.94%, globulin 2.63%. Blood urea 304 mg.‰.

X-rays: All the bones were examined and showed slight generalized osteoporosis. Calcification of small vessels (fig. 2), particularly in hands and feet, and calcification of the subcutaneous tissues above each ankle (fig. 3). The kidneys showed no calculi nor metastatic calcification.

Fractional test meal: Normal.

Histology [H. and E. stain].—Little change in horny layer. Very darkly stained granular layer, especially near "acneiform papule" (fig. 4). This shows a horny plug, above many polymorphonuclear cells and calcium particles, much debris, and many large eosinophil bodies surrounded by irregular spaces. Relatively large calcium deposits in the corium with little inflammatory reaction about them (fig. 5).

Silver nitrate stain: Numerous fine black granules in epidermis, most marked in the basal layer (fig. 6). On treating another section with hydrochloric acid these granules were found to be much less numerous, suggesting that many of them are calcium. The larger deposits of calcium in the corium are seen to be made up of two elements (fig. 7): (1) Amorphous masses. (2) Collections of band-like deposits looking like the "perished rubber" appearance seen in pseudoxanthoma elasticum. This suggests deposit of calcium about the elastic fibres.

Dr. Donald Hunter: This case is more likely to be one of chronic nephritis with secondary hyperparathyroidism than one of primary hyperparathyroidism. The evidence in favour of this is that the renal insufficiency is already advanced, X-rays show no evidence of metastatic calcification of the kidneys, and the bone lesions are slight; there is neither deformity nor cyst formation. Exploration of the neck is not to be advised and, indeed, the girl is dying.

POSTSCRIPT.—This patient died six days after the meeting, and necropsy revealed chronic nephritis with great shrinkage of the kidneys. There was hyperplasia of all four parathyroid bodies.

[See Plates I and II.]

[It is intended to publish the case fully at a later date.]

Pigmented Birth-Marks Treated by Thorium-X.—F. S. AIREY, M.R.C.P.E.

Photographs were shown to illustrate in natural colour the results of the application of thorium-X to simple pigmented marks. Case records gave details of the dosage and frequency of treatment, which, in some instances, covered a period of years. The response varied but, in several cases, Dr. Airey considered that complete and permanent disappearance seemed likely.

He said that pigmentation of the adjacent skin was a common sequel of thorium-X treatment in parapsoriasis, scleroderma, &c., especially on parts normally covered. It had been attributed to the disintegration products (thoron in particular) and could persist for some time. Depigmentation of a treated area was equally frequent, especially in dark-skinned people. Recovery of pigment was customary, but might be slow. His observation of this process had prompted him to experiment with simple pigmented marks.

He could not say why improvement occurred, but suggested ionization as a possible explanation. The mere migration of pigment to the periphery was not acceptable to him, since it seemed not to occur. Perhaps the mechanism was repeated exfoliation. He invited suggestions to account for the dual action of thorium-X on pigmentation and, in particular, for its effect on pigmented naevi.

Whilst in no instance had he observed any adverse effect, he wondered whether it was allowable, or even wise, to treat cosmetic blemishes by this means; for pigment-bearing cells were submitted to the powerful ionizing effect of alpha particles and disappeared. He felt this might invite trouble and was uneasy about malignant melanoma, although no mark was touched which gave any indication of pre-malignant or malignant change. It was easy to condemn a method. The subject was worthy of careful thought.

Dr. P. J. Feeny: Peripheral hyperpigmentation is not an inevitable sequel of prolonged treatment of a lesion by thorium-X, as witness two of the cases I am showing to-day. I suggest that the peripheral pigment in Dr. Airey's cases was transferred from the mole.

Dr. C. H. Whittle, replying to a question as to the experience of members with malignant changes in pigment moles, said: I think it will prove extremely difficult to assess the incidence of malignancy in pigmented moles because of the possible long latent period before secondary deposits may appear. If a parallel can be drawn between melanotic tumours of the eye and the skin it is possible for metastases to appear in distant organs, such as the liver, as long as twenty-five to thirty years after removal of the primary tumour. The follow-up of these cases over such a long period presents obvious difficulties and late metastases are very apt to be missed. It seems unlikely, however, that such cases are numerous.

Three Cases of Port-wine Stain Treated by Thorium-X.—P. J. FEENY, M.B., B.Ch. (for A. BURROWS, M.D.).

(1) Girl aged 17. Port-wine stain on lower lip and chin. A photograph showing the extent before treatment was shown. This case had been treated once a fortnight for the previous seven months with thorium-X 1,500 c.s.u. per c.c. in varnish. Two treatments had been missed, and, on both occasions, it had been noticed that the naevus became paler during the second fortnight. The naevus was now half its original size, was paler and appeared to be breaking up into islands.

(2) Child aged 2½ years. Port-wine stain on thigh. Painted 20 times in past fifteen months, the first dozen times with the 1,000 c.s.u. strength and the rest with the 1,500 c.s.u. strength. This naevus was now very much paler, but not reduced in size.

(3) Child aged 1¼ years. Two port-wine stains were present when painting with thorium-X was commenced at the age of 3 months. One extended from the root of the nose more than half-way up the centre of the forehead and above the right eyebrow as far as the level of the outer canthus; the other, on the nucha, was the size of a shilling. Both were painted four times during the next four months; the 1,000 c.s.u. per c.c. was used first time and the response after a fortnight was noticeable. The 1,500 strength was used subsequently. Both naevi disappeared after the fourth painting.

There were no cavernous naevoid excrescences in any of the three cases.

Dr. F. S. Airey: Thorium-X appears to be the remedy of choice in port-wine stains in infants, when the vascular tissue seems to be most responsive. In older children and adults improvement is often so slow, in comparison with that following alternative methods (such as carbon-dioxide slush), that one doubts its real value. Results undoubtedly can be achieved, but they are by no means dramatic.

I have been using thorium-X for this purpose for about ten years with, on the whole, encouraging results. In some instances, complete disappearance has been achieved, but when unsuitable cases are undertaken their slow progress leads to pessimism. I have seen no real ill-effects from long-continued use, apart from slight atrophy and telangiectasia sometimes, in which the skin of the treated area develops a glazed appearance. The chief virtues of the remedy are simplicity, safety and painlessness.

I feel that Case 3 (shown by Dr. Feeny) would have resolved spontaneously; for this type of symmetrical telangiectatic hæmangioma, situated over the glabella and upper eyelids, is relatively common, and seldom, if ever, persists beyond infancy.

Dr. Goldsmith: I have found thorium-X very efficacious for port-wine stains in adults.

The President: I agree that the results in selected cases are very good.

Dr. F. J. Feeny: The cases shown were treated intensively by choice, as I did not fear any possible sequel from 99% alpha radiation apart from sequelæ already known. I think it is useless to treat with thorium-X cases with nævoid excrescences or cases infiltrated with fibrous tissue. I would not expect good results if treatment were commenced after adolescence.

Pemphigus Vulgaris, Showing Arsenical Pigmentation.—P. J. FEENY, M.B., B.Ch. (for A. BURROWS, M.D.).

Boy aged 5. The lesions had begun two years previously and had been appearing almost daily without intermission since. Pustules on an erythematous base and erythematous-vesicular plaques were present on the circumoral area, the neck, hands, fronts of the thighs, scrotum and penis. There were no buccal lesions. There was well-marked arsenical pigmentation of the trunk. Very few bullæ on normal skin were present, but bullæ the size of half a crown had been present and had been scratched and infected by the child. The degree of itching was difficult to assess in a child of this age, but it appeared to be moderate.

Investigations (Dr. Spink) showed a 6% eosinophilia; from the stools *Proteus vulgaris* had been cultured and, from the lesions, diphtheroids and *Staph. pyogenes*, the latter sensitive to penicillin.

This case was now on Suramin B.P.C. While awaiting the final diagnosis, sulphonamides, penicillin cream, stock *Staph. pyogenes* vaccine and daily general ultraviolet ray therapy had been without effect.

Dr. P. J. Feeny: I am prepared for an alternative diagnosis of dermatitis herpetiformis; such a case should be watched for a long time before making up one's mind. Two further investigations which might help are the response to provocative iodides and a Pels Macht test.

Dr. A. M. H. Gray: I am quite familiar with this type of case and have had about 12 cases, mainly at Great Ormond Street or Goldie Leigh Hospitals. Though the disease often lasts a long time the prognosis is good. Two of my cases were lost sight of before they were cured; there is another one under my care now, the remainder have cleared up. I feel sure the cases are not pemphigus vulgaris and I do not think they are dermatitis herpetiformis. The distribution is fairly characteristic: though there may be blisters over most of the body, they tend to be most numerous around the nose and mouth and on the hands and feet. The first case I saw many years ago had a persistent nasal discharge and in view of the distribution of the eruption I had thought the nasal discharge might be responsible for the lesions. The lesions did, in fact, clear up in a few months by using nasal irrigation of 1% chloramine T in an alkaline wash. None of the other cases in which I have tried the treatment responded. None of my cases have shown any marked response to arsenic, but the one now under my care does seem to be responding to sulphathiazole. On the other hand, another case treated with sulphapyridine has not improved. I have not so far found any specific remedy for the condition but with careful nursing the cases do appear to recover spontaneously.

Dr. Wigley: I remember that Dr. Sequeira usually did not commit himself in such borderline cases, labelling them "bullous eruption".

The President: Has anyone known a case to end fatally?

Dr. Forman: These cases go on for perhaps ten years and then recover.

Dr. A. Burrows: I recall a case which had been an in-patient for so long that it grew up and had to be transferred to an adult ward.

Pigmentation. ? Pellagra.—A. C. ROXBURGH, M.D.

Mrs. E. B., aged 53. A well-covered woman at the menopause who for five to seven years has had periods of indigestion every three to four months. During these periods she has lived on a very restricted diet of cereals and milk with vegetables only three times a week and no liver, kidney, meat, eggs, fish or cheese. After being on this diet for seven weeks continuously she was admitted to Wellhouse Hospital on 16.10.44 complaining of "burning", irritation, redness and pigmentation of face. Paræsthesia of fingers and arms up to elbows and toes to half-way up legs.

On examination.—There was dark, fairly even, pigmentation of face with underlying erythema, mottled pigmentation of neck and anterior chest wall and under breasts. Some pigmentation of hands and wrists. None of nipples. No mucous membrane lesions, no diarrhœa, no giddiness. No warty growths to suggest acanthosis nigricans. Nothing to suggest Addison's disease. Pulse 90 regular, B.P. 174/100, later 144/108. No symptoms,

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discharge. There were similar but smaller lesions on the lower limbs, four in number. The boil on the cheek had been the first to appear: this was in December 1943, just before he left Baghdad for England. It remained a single lesion until June 1944. It was a considerable annoyance but nothing more: there was hardly any pain and no effect on the general health. In June the other lesions appeared, all within a few weeks of one another.

Laboratory examination: Leishman-Donovan bodies in great numbers. W.R. negative.

Treatment.—All lesions were treated by the application of antimony tartrate 1% ointment, but there was no effect from this in six weeks. The lesion on the face was also given 400 r, X-rays. This produced a dusky induration with perhaps increased tenderness, but it began to heal after a month and now there is very little trace of there having been anything the matter with the cheek.

In August 1944 he was given intramuscular injections of myocrisin, about 6 of 0.02 g. each, and very soon all lesions healed up. There is considerable superficial scarring in all lesions, though very much less in the case of the boil on the cheek.

After-results of Treatment of Severe Lupus with Finsen Light (8 Cases).—A. BURROWS, M.D.

These cases of lupus vulgaris illustrate how good the results of treatment may be, even where the disease is advanced. Seven of them are also in contrast with the only male patient, who has a recurrent nodule in a nasal skin graft.

There is some criticism of the use of Finsen light in such cases; it is said that it is only valuable in the early condition, but these patients show the results which can be obtained in later cases.

The President: I think we should all like to congratulate Dr. Burrows on the results of the treatment of these lupus cases. I found on inquiry that many of them were able to go to the London Hospital every day for general light treatment and perhaps once a week or fortnight for the Finsen treatment, which no doubt explains the good results.

Dr. Burrows: In some of these cases it was possible for the patients to have general light treatment at home, coming up to hospital for Finsen light. The length of time the treatment took varied; some cases would be clear in a year and others in two or three years. In the early stages a few were on Finsen light, but the majority have been treated with the Lomholt lamp.

Verrucose Dermatitis of Amputation Stump.—L. FORMAN, M.D.

Miss F. P., aged 42.

November 1933: Amputation through middle of thigh for sarcoma.

First seen October 1941. Fourteen months previously skin noticed to be weeping over stump and an infective dermatitis was diagnosed. Cultures gave heavy growth of *Staphylococcus aureus*.

December 1942: Skin over stump was warty with filiform projections, covered with thick, soft horn which easily detached.

Section (January 1943): Epidermis acanthotic and parakeratotic. Papillae long and narrow and containing dilated capillaries and lymphatics.

Treatment.—Fractional doses X-rays.

This case recalls the verrucose dermatitis seen in elderly, neglected patients on the feet and lower legs. There is usually considerable oedema. The verrucose condition not infrequently commences along the dorsal aspect of the toes, where the skin is pinched by the adjoining toes and the shoe. It is found in patients with circulatory failure, where the skin has not been kept clean, and appears to follow an infective dermatitis of the skin.

This patient wears a false leg which cups the stump, probably producing a mild degree of lymphatic obstruction, and the skin has become acanthotic and verrucose following infection.

Dr. E. W. Prosser Thomas: I showed an elderly patient at the Section in 1942 in whom the ankle and lower third of the leg was involved in this kind of warty change (*Brit. J. Derm. Syph.*, 54, 242). There was no circulatory failure or obvious oedema suggestive of lymphatic blockage. The basis appeared to be a low-grade infection locally in the skin as it had been possible in the early stages to express a small amount of pus from the warty area and it was associated with a smouldering inguinal adenitis. The condition has been described under the name *pachyderma vegetans* (Wiederhold, G. (1940) *Derm. Wschr.*, 3, 1039).

Dr. H. Stannus: The condition resembles that produced by a filarial infection which obstructs the lymph circulation.

or signs referable to central nervous system. Blood picture, E. S. R., urine, W.R., plasma chlorides and blood sugar, all normal.

Fractional test meal: No acid in first four specimens. Very slight rise (to 10 c.c. decinormal sodium hydroxide) after 50 mg. of nicotinic acid.

Barium meal: No evidence of any gastric or duodenal lesion. No delay in emptying.

Treatment.—High protein diet including meat, eggs, vegetables, milk and fruit. Nicotinic acid 50 mg. ten times a day. Aneurin 12 mg. three times a day. Adexolin 10 drops three times a day in milk. No tea. Acid hydrochlor. dil. 30 to 60 m after meals (now on m 30 before meals and m 60 after meals).

Progress.—Still gets indigestion. "Burning" and paræsthesia decreased but occasionally present. Very little change in pigmentation after three weeks of above treatment.

Dr. Stannus: This is a most interesting case in regard to the differential diagnosis, but I think one could say definitely that the condition is not pellagrous.

Dr. A. N. P. Milner: Recently I saw a case of what I took to be Riehl's melanosis. The pigment was distributed on the sides of the forehead, face and neck and passed down over the sternum and underneath each breast. Over the sternum it had a mottled appearance. The pigmentation was rather a coffee colour, not so dark as in the present case. There was hirsuties of the upper lip and thighs and some tendency to male formation of the pubic hair.

I thought the condition might be due to a lesion of the adrenal cortex and sent her to see Mr. Broster. Urinary androgens were estimated, and, although raised, were not considered high enough for a pathological adrenal cortex. At laparotomy the adrenals were found to be normal in size.

I treated her for six months with hexoestrol tablets, 1 mg. twice daily for the first fourteen days of the menstrual interval and with 0.5 c.c. synapoidin thrice weekly intramuscularly for the same period.

The treatment was continued for six months with marked improvement in the general health and considerable reduction in the degree and area of the pigmentation.

Pigmentation of Face.—A. C. ROXBURGH, M.D.

Miss J. W., aged 38. W.V.S. organizer. First seen at St. Bartholomew's Hospital August 13, 1944. Had then had for one year erythema, pigmentation and scaling of nose, one month erythema pigmentation and scaling of rest of face. Face was pigmented a fairly uniform dark brown with an underlying erythema and slight scaling. There were pigmented greyish papules forming lines on the lower eyelids. There was no pigmentation of the neck, hands or elsewhere. Lack of pigment on hands not due to wearing gloves. No soreness of mouth or tongue. Scalp sometimes scurfy. No giddiness, or diarrhoea or other symptoms. Patient was then very tired and in need of a holiday. She had taken sedormid off and on in small amounts for nine months. Had never worked with oil, used no eau de Cologne or other scent on face. Had no dietary fads, ate everything that was going. Periods regular and, apart from being tired, was well. Urine normal. B.P. 145/90.

X-ray reports, August 1944: Chest—no obvious lesion; teeth—some caries and some apical infection; sinuses clear. Told to stop sedormid and to take a holiday. Went to Inverness for one month, from September 21 to October 21 approximately, and says she nearly lost her pigmentation while away except under the eyes, but it returned in two hours after returning to her office! Office centrally heated and poorly ventilated. While in Inverness had had a salicylic and ichthyol cream for face and salicylic and sulphur ointment for scalp from Captain Lipman Cohen. When seen October 25, 1944, was much as before. Then put on 500 mg. of nicotinic acid daily. She has now taken this for three weeks and pigmentation is definitely decreasing.

Diagnoses considered: Lupus erythematosus; sedormid eruption; pellagra; Riehl's melanosis.

The President: I do not think this can be a case of Civatte's poikiloderma. It is all over the central parts of the face and not in the areas usually affected by that condition.

Dr. W. N. Goldsmith: Riehl's original cases were thought to be due to the ingestion of petroleum or other food adulterants. In Vienna Oppenheim described melanosis due to lubricating oil. Civatte at first ascribed his poikiloderma to adrenal trouble; but in 1933 he wrote to me that he had come to the conclusion that these cases were the same as the first cases of Riehl, but he was sure that his cases, and probably several of Riehl's, were not due to tar. Hoffmann and Habermann suggested that even occupational tar or petroleum melanosis might be brought about by inhalation or even ingestion, rather than by external action. I have just seen such a case in a coalminer.

Cutaneous Leishmaniasis.—H. CORSI, F.R.C.S. [*In absentia*].

The patient was first seen in July 1944. On the left cheek was a brawny swelling, eroded in the central part, and exuding a serous discharge. Over the left olecranon was an infiltrated area nearly 2 in. in diameter with superficial ulceration and a serous

Section of Radiology

President—J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

[November 17, 1944]

DISCUSSION ON POST-WAR ORGANIZATION FOR THE TREATMENT OF CANCER

Sir E. Rock Carling: Radiotherapists have a dual role with surgeons in the treatment of cancer, and any organization to be effective, must be adapted to both dispensations. This fact became evident when tentative efforts in several parts of the country to promote schemes under the Cancer Act, were sent up for approval by the Ministry of Health. It then appeared that for administrators, and others without our special knowledge, the true picture of what was needed for a complete organization had been distorted and obscured by the existence for many years of an official body—the Radium Commission, which had established national centres in all the university cities (except perhaps London) and regional centres in others—23 in all. It was necessary to explain that though an organization for the treatment of cancer by one means already existed upon a regional basis, cancer schemes under the Act could not be limited to radiotherapy but must provide for diagnosis and for treatment by surgery.

Radiation is, for the most part, conducted by whole-time staff; surgery very largely by part-time. Whilst radiation is on the whole concentrated in comparatively few places, surgery is distributed over many. One set of circumstances lends itself to a simple and tidy administrative job; the other presents many difficulties.

Those most conversant with the problem as it affects the whole country are agreed that radiotherapy should be concentrated in a few fully equipped and strongly staffed institutions, each perhaps with a very small group of associated subcentres. For reasons which are common to both systems of treatment, the headquarters should be in a university city. A single radiotherapeutic organization can deal with a population up to three and a half or four millions; two millions form a satisfactory number; sparsity of population makes it necessary to provide for an area with as little as a million as a minimum. Does such a partition of the country suit a surgical organization?

There is evidence to suggest that for *all* hospital purposes the country, outside the London area, can be divided suitably into about a dozen major areas, each with a university centre as its natural headquarters. Within these major areas, called "Regions" for convenience, though not necessarily co-terminous with the Civil Defence Regions, smaller districts can be discerned, compactly focused upon county boroughs with a surrounding hinterland served by converging roads and railways. Hospitals, generally speaking, follow the same siting and grading as cities and towns. The surgical resources of such areas, with populations of say a quarter of a million, should be quite adequate for well over 90% of surgical requirements, including, of course, those for cancer.

There is a fund of experience, of the dispersal over these "districts" and these whole "regions", of skilled and expert services based on the university cities. They exist for orthopaedics, neurosurgery, thoracic surgery and tuberculosis, plastic surgery; for pathology and blood transfusion; as well as for faculties such as veterinary medicine and technical education.

We know, then, that a radiation service for cancer requires a large area for its most successful development; we know that special branches of surgery can operate with hitherto unrealized success over the same areas. In my opinion they can be utilized with equal success for the surgery of cancer, and can parallel the organization for irradiation. The time is ripe for just such development.

When we come to consider the organization a little more closely, it is I believe a useful and a wise plan to think from the periphery of a region inwards. The Cancer Act provides for those suffering from or suspected of cancer. The suspicion of cancer arises in the ambit of the general practitioner. Preliminary investigation centres should therefore be within reasonable immediacy of the patients' homes. When we function. Such centres will be needed in cities because even in the heart of them there are parts in one sense peripheral. Suspicion once aroused must be dispelled; to do that

Pseudoxanthoma Elasticum.—E. W. PROSSER THOMAS, M.D.

Mrs. F. G., aged 20, first noticed a change in her skin when she was 16. Beginning at the sides of the neck it has slowly extended downwards over the clavicles and across the mid-line, so that most of the neck is now involved. The skin is smooth and soft but is uniformly divided into tiny linear and oval xanthelasma-like areas interspersed with telangiectases, which give it a yellowish-lilac colour. Loss of elasticity is well shown when she turns her head to one side, the skin then falling into longitudinal folds.

There is no history of any similar kind of skin disorder in other members of the family and her mother and father are not blood relations.

Eye surgeon's report (Mr. T. M. Tyrrell): "There is a small patch of choroiditis near the disc in the upper part of the right fundus. This may be a retinal mole. There are orange streaks all over the upper part of the right fundus and to a lesser extent in the left fundus, which are very similar in appearance to angioid streaks."

Radiography: Chest: No evidence of lung lesion. Pituitary fossa: Small rounded bridged fossa.

? Toxic Melanodermia.—H. J. WALLACE, M.D.

E. H., aged 62, housewife. About seven years ago a few lesions developed on the face, red in colour, apparently about 1 mm. in diameter. These disappeared and about five years ago brown pigmentation began around the neck, gradually spreading over the shoulders, body, and lastly over the legs and arms. A fine desquamation has been present throughout, together with mild irritation.

Nothing relevant in her past or family history. No history of undue contact with tar, oil or vaseline or of administration of arsenic or gold. Normal menopause at the age of 50. General health excellent.

On examination.—There is well-marked and widespread melanodermia, together with some fine desquamating erythrodermic areas. The pigmentation, which varies in colour from brown to brownish violet, predominates as lichenoid lesions mostly arranged in a reticulate pattern. Some of the lichen papules are shiny, others of a mat surface with desquamation. The areas around the hair follicles are not free of pigmentation. The pigmentation is most marked on the chest and back but is also present on the legs. The anterior aspects of the patellæ and the tibial tubercles appear to be the only areas free of pigmentation. There is no pigmentation or lichen on the mucous membranes of the mouth or vulva, and relatively little pigmentation on the face. The appearance in some areas suggests early atrophy. There is no abnormal pigmentation of sclerotics or of retina.

She is of a nervous temperament but there is no evidence of organic disease in any system. Examination of the blood showed no abnormality and a Wassermann test was negative.

Histological examination shows the greater part of the pigment to be in the dermis, where some of it is in cells of the nevus type, the remainder being contained in phagocytes. There is also a chronic inflammatory cell infiltration of both the dermis and epidermis.

Dr. Gray: I thought this might be a case of *parakeratosis variegata*. It is much more pigmented than those usually described but it has the reticular pattern composed of lichenoid lesions which are so characteristic of this rare condition. It is, of course, sometimes known as *parapsoriasis lichenoides*.

Telangiectasia Macularis Eruptiva Perstans.—CLARA M. WARREN, M.R.C.S., L.R.C.P.

Mrs. R. M. M., aged 42, shows all the features of this skin condition, previously described by H. W. Barber and F. Parkes Weber ((1932) *Internat. Clin.* 4, 71—76) and by others. She is obese; her colour is high, from a marked dilatation of the capillaries of her cheeks. She shows macules in clusters, oval in shape and copper-coloured. These are most typical on the neck, and have been present for two years. The urticaria with pigment is seen on arms and trunk. Darier's sign is present. Itching is only a feature when dermographism and anorexia are present. Urticaria on the right forearm has been present for six years.

Other features include recurrent herpes of the mouth, and irregular menstruation for the past year.

The blood-count is normal.

Dr. F. Parkes Weber: It is certainly a very fine example of what has been described as *telangiectasia macularis eruptiva perstans*. The special feature to be noted is that in this case the urticarial factor has been very marked.

a clear idea before he starts of the total dose of radiation the patient is to receive, whatever the source and whatever the fields; it is not enough to administer to a lesion a dose which leads to its clinical disappearance. Whoever implants ought to have such knowledge of the fields induced by complicated sources as will enable him to secure homogenous irradiation; he must submit the field he has in fact produced to analysis by a physicist, and be ready to correct it; he must co-operate with the radiotherapist in supplementary irradiation from external sources. The gynaecologist who has completely familiarized himself with the physical basis of irradiation and who, like the radiotherapist, will submit his given case to scrutiny by the physicist, is entitled to carry out insertion of appliances.

The life of Medicine is bound up with research. There is no standing still; advance and flourish or stagnate and sink to a dead level of mediocrity. Research is mainly concentrated in universities and for the purposes of cancer treatment there ought to be close association with the departments of pathology, biology, physics, chemistry, genetics, anatomy, physiology, pharmacology and veterinary science. There is no branch of science which may not touch our problems at some point, and there is no question as to the propriety of establishing area headquarters in the university vicinity. So far as radiotherapy goes, the advances in prospect, in the development of apparatus, make it imperative that the establishment should be where expert staff is available in quantity and quality. The universities are, of course, the natural gathering place of medical professional groups and associations.

All this does not imply that research cannot be carried on in other parts of a region. On the contrary we want to see all the principal institutions of the "districts" and their staffs, so integrated that their research worker, if his work establishes a claim, has, of right, the co-operation of the Central Research Department, just in the same way that the clinical staff should feel themselves part of the total resources of skill in the area service, with access as of right to the Central Faculties, institutions, departments and personnel. Such a relationship has been successfully established in another field, in at least one area, and should become universal. Again, the passage should be two-way. The staff of divisional hospitals ought to welcome members of the headquarters' team for the friendly help they can give and take, and put their cases at disposal for co-operative research.

I need do no more than mention two or three other requisites of a successful organization. One is the importance of organized training for all types of technical assistants, including nurses under that term. The other is the provision, not only of "clerical assistance", but of secretarial aid by highly educated and trained staff of status that demands a substantial salary. The word "clerk", which in official departments often means "filing-clerk" at a weekly wage, should not be used when "secretary", with the connotation "personal assistant" is intended.

In attempting to formulate a cancer scheme we must be actuated solely by the interests of the patient. The test question for us is: "What would you consider the best possible arrangement for the treatment of your own most intimate dependants or for yourself?" If the answer involves some infringement of the right of every medical man to pursue his own course and to treat every patient he thinks he can manage, will that infringement in the end damage the reputation of the profession or constitute an unwarrantable intrusion upon our liberties? At any rate, we must try and educate the public to accept nothing less than the best available, and see that they know where to get it.

Mr. George F. Stebbing: In the United Kingdom in 1942, the following deaths were due to cancers: 7,887 breast; 5,097 uterus; 1,206 larynx; 1,033 tongue; and 290 lip. This state of affairs exists because we have failed to create an organization that will make the best use of the abilities we possess, the instruments we have devised and the resources we control. The Cancer Act, 1939, recognized the necessity for nation-wide co-ordination of effort, but so far, in spite of the efforts of the Radium Commission, little has been accomplished for the following reasons:

(1) Since the beginning of the century science and industry have provided us with a great variety of implements and methods the proper use of which enables us to make many diagnoses of early disease which could not be made by the older methods; but the use of these implements and methods require for their proper use not only a good deal of equipment, which few general practitioners possess, but also knowledge and experience that no one man possesses but can only be found in a team of specialists. Many doctors working under the National Health Insurance scheme, and particularly in large towns, have to see so many patients in a short time that they cannot find time for the careful consideration of obscure symptoms.

(2) The number of hospital beds and the facilities available in outpatient depart-

requires all the diagnostic resources of a polyclinic, that is, of a consultative out-patients' department as distinct from an Accident and "Casual" department. Diagnosis is the function of the large general hospital. Once diagnosed, the cancer patient should be treated in the principal hospital of the "district", only being sent on to the special department of the headquarters' hospital centre if that help is necessary or expedient.

Although the flow of patients should be from the periphery towards the centre, with careful filtration *en route*, so that the autonomous sufficiency of the intermediate hospital is not neglected, the traffic should be two-way—that is to say, the most expert H.Q. help should be at the service of the "district" associates—and that of *their* staff at the service of the general practitioner.

In the principles laid down by the Minister's Sub-Committee on Cancer, a plan is proposed for a Headquarters' Team, selected from the most highly experienced surgeons, physicians, specialists, radiotherapists, pathologists and physicists to be found in the "region". Headquarters should not be thought of as a dominating or direction-issuing body, but as *primus inter pares* in relation to its associated divisional partners. There are in being regional organizations for radiotherapy where such a headquarters' staff (when at its full strength, out of wartime) can and do visit "district" institutions to consult with the local surgeon-specialists, to decide by agreement upon the most suitable form of treatment for each and every case. It is of equal importance that the experience of the most highly skilled surgeons, specialist-surgeons, physicians, physicists and pathologists should be at the disposal of the "districts" when needed.

The conception of the team envisages a service of consultant specialists whose locus, but not necessarily whose domicile, shall be at headquarters in the university city, but no one should be excluded simply because he does not practise in the metropolis.

All others serving directly the purposes of the organization will constitute the panel, and they likewise must be selected, for it will not mean every medical man in the region, it will mean those who hold sessions at an approved clinic. Selection for team and panel will obviously be an invidious and very delicate job.

It will be generally agreed that operation for cancer of a given region of the body ought to be in the hands of those whose daily practice is in that region; that cancer of the central nervous system should go to the neurosurgeon; of the bronchus to the thoracic surgeon; of the abdomen, stomach and intestines to the abdominal surgeon, and so on. We can all concede that the field of the gynecologist is now defined. I think it is true that the results obtained at a hospital devoted entirely to diseases of the rectum, in operations for cancer of that part, are better than those of most "general" surgeons. It reflects the enormous advantage of extensive experience. I do not doubt that there are men of such competence that they could shine in every special department, but in fact, limitations of time would and do seriously contract their experience if their efforts are too widely diffused, so that in practice we find men of the most brilliant accomplishments confining themselves to one field.

I suggest that those with a high local reputation for skill ought to have the opportunity of exercising it in bigger institutions, the resources of which would afford fuller scope for their talents. At any rate, major surgery should not in future be done in institutions where there is no resident; where the pathological and radiological services are second-rate; where collateral specialists cannot be met at will.

We now come to another aspect of the same question. Under the Cancer Act, and under the anticipated legislation which is likely to absorb and supersede it, payments are to be made from public funds. It would be contrary to all experience if those charged with the expenditure did not ask for some assurance of the competence and experience and wisdom of those entrusted with the treatment of the cancer cases coming under the scheme. They may be satisfied with a very low standard and accept everybody—every qualified man—as in fact the law does. But is that what we as a profession want? Is it good enough? Of course it is not, but we must see to it that selection of men for Team and Panel is based on the best professional advice obtainable, and whatever co-ordinating committee may be found necessary to integrate regional plans, it should be under an obligation to seek expert advice in such matters.

Whilst a framework for organization may be centrally proposed for the country as a whole, in the regions themselves the pattern is to be filled in as best suits their local condition and resources. Different plans may be propounded for dealing with difficult problems such as staffing, and may be worked with equal success.

The radiotherapist ought to be consulted about every case. It is true that to-day he plays a minor or negative part in some fields, but who knows when the cyclotron or the betatron or other extremely high voltage sources may not bring cancer of the stomach or the rectum, or the liver within the range of practical use? This brings us to the question "who should do radium implantation"? Whoever does it must have

a clear idea before he starts of whatever the source and whatever a dose which leads to its clinical knowledge of the fields induced by homogenous irradiation; he must by a physicist, and be ready to supplementary irradiation from external familiarized himself with the physicist, will submit his given case to the insertion of appliances.

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(2) The number of hospital beds and the facilities available in outpatient depart-

ments have been quite inadequate in almost all parts of the country for the number of patients they have to serve.

(3) When the patient is admitted to hospital we are faced with a curious situation: although cancer is the second commonest cause of death it occurs in so many situations and such different forms that each type becomes a disease in itself, and may be a rare disease, so that by no means all practising surgeons and radiotherapists can become experienced in handling each type of disease, and in few places are there any arrangements to ensure that the material available is so distributed that all the people treating it are really expert.

(4) Radiotherapy plays an important part in the treatment of cancer, and in many hospitals there is neither an efficient radiotherapy department, nor an established arrangement for obtaining radiotherapy elsewhere.

(5) The laity in general have a dread of cancer, which leads them to delay examination or to concealment of the disease.

We must have available in every region a cancer organization that is known to every medical practitioner, that is freely and immediately at the disposal of every patient, and that is so arranged that it ensures efficient diagnosis and prompt treatment for every patient. Dr. Malcolm Donaldson has recently published a paper describing a scheme for the organization of the diagnosis and treatment of cancer in London and the Home Counties, and it is along such lines that we shall have to proceed.

There should be a regional organization with a whole-time director that should serve the needs of a population of about two million people. The headquarters of the organization should be in a general hospital where there is a highly organized radiotherapy department, and where physicians, surgeons, E.N.T. surgeons, gynecologists, radiodiagnosticians, pathologists and physicists can consult frequently, and have time and opportunity to discuss the problems of the work in which they are engaged. At all large hospitals there should be such diagnostic and follow-up clinics attended by members of the headquarter staff.

The records of the organization must be distinct from the hospital's case papers, must provide (a) a record of the patient's condition from time to time so that an estimate may be made of the changes that have taken place since the last visit, (b) accurate records of the treatment as a guide for further treatment when needed, and (c) a basis for statistical analysis of the results obtained by treatment.

Both "voluntary" and "local authority" hospitals must take part in each organization.

Dr. Donaldson has pointed out that if the needs of the Home Counties are to be considered, London and the Home Counties will have to act as one area, and should be divided out sector-wise, each sector having its apex in London at one or more teaching schools, and its base at the periphery of the Home Counties.

Each cancer organization must have its own council and management committee, the former being a sub-committee of whatever type of joint authority that may materialize in the formation of the National Health Service, and the latter (the management committee) being composed of professional representatives of the hospitals taking part. The financial arrangements of such an organization should present no difficulties, since all the services rendered will be a part of those provided under the National Service Scheme. The facilities of the organization should be available to private patients under suitable financial arrangements.

What difficulties have to be overcome to bring such organizations into being? The main difficulties are vested interests in existing arrangements, and the dislike voluntary and local authority hospitals have for co-operating with each other. These difficulties can be surmounted, and one of the best means of surmounting them is the provision of discussions such as this which I should like to see repeated in every medical society and every local authority in the Kingdom.

Dr. John R. Nuttall: Approximately 45% of patients are beyond any curative treatment when they first seek the advice of the specialist, due to ignorance and fear on their part, and, to some extent, lack of knowledge of the disease amongst general practitioners.

Any service for the treatment of this disease, which invades almost every branch of medicine and affects all groups of the population, must be both medically and regionally comprehensive. It must provide readily accessible facilities for diagnosis, competent surgical treatment and radiotherapy, and an organization for the nursing care, in home or hospital, of those for whom active treatment is no longer possible. This implies for every million of population the provision of a number of diagnostic clinics, and facilities for the treatment of some 600 surgical, and 700 radiotherapeutic cases per year, requiring approximately one hundred hospital beds for active treatment alone. It is generally recognized, however, that to be efficient and economical, cancer-treating

units should serve a population greater than one million—two to three millions being considered more satisfactory. A comprehensive service for such large and often widespread population groups calls for elaborate organization, and it appears logical that the Ministry of Health should take a very active part in it.

The provision of cancer clinics strategically placed throughout the area to be served, with arrangements for admission to hospital for special examinations, would appear to provide diagnostic facilities. The problem, however, is complicated by the fact that a wide variety of medical specialities is involved in cancer diagnosis and treatment, and it is frequently impracticable to provide all these specialities in every clinic hospital at one time. In the large centres personal collaboration is possible, in the smaller it is bound to be restricted. It follows, then, that the organization of clinic services should be so devised that it is immaterial whether surgeon, specialist or radiotherapist first sees a case, for if not obviously within his sphere it will automatically be passed to the competent authority or be the subject of collaborative consultation. Radiotherapists should have a good knowledge of cancer surgery, and surgeons of the possibilities of radiotherapy. It is probable that in any cancer unit a number of beds should be provided, to which any member of the staff who deals with cancer may admit cases for collaborative investigation without encroaching upon the beds set aside for active treatment.

The pathological services should be in the hands of specialists in tumour histology. Departments should be organized to provide reports in two to four days after biopsy, for the choice of treatment frequently depends upon the histology of the tumour, and its inception has to await this information. It is probably unnecessary that all examinations be made in a central pathological unit, but it is desirable that every slide should eventually pass through that unit, so as to ensure wide experience for the specialist pathologist, and uniformity of opinion for the clinician. The usefulness of aspiration biopsy should be taken into account in building up the pathological unit for a cancer centre. Where they are separated, close co-operation between the university and cancer scheme pathological departments should be maintained.

Treatment.—There is much to be said for the centralization of all cancer surgery in the hands of the staffs of the major hospitals and even for personal specialization within these staffs, for cancer surgery is usually major surgery calling for experienced judgment and high technical ability. It is sometimes objected, however, that the creation of purely cancer surgeons would, in the long run, lower the standard of diagnosis by creating minds which see cancer in everything, although it raised the level of operative judgment and technique. The present trend towards anatomical regionalization in general surgery may offer the best solution of the surgical problem.

There are two spheres of cancer surgery which closely affect the radiotherapist, radical mastectomy and block dissection of the neck. The former is probably the most misused operation of those who merely practise surgery as an interesting relief from general practice, and as such is productive of innumerable tragedies which the radiologist is called upon to salvage. In this case the main trouble lies in failure to know when not to operate rather than in faulty technique. Block dissection by an expert offers the best chance of cure of secondary neck glands, but many surgeons will not attempt it and experts are few. As a radiotherapist I hope that future cancer schemes will deter the over-enthusiastic from radical mastectomy in inoperable cases, and will provide more facilities for block dissection.

Radium and X-ray treatment are so alike and so co-involved that they should be organized as one entity—radiotherapy. For economic reasons a radiotherapy centre should serve a population of at least two millions. Considerable centralization of treatment is essential, for in this branch of medicine expensive and elaborate equipment is as important as personnel. Various methods of partial decentralization are in use—the major unit sending staff to local hospitals to carry out treatment; association for some types of treatment between the local radiologist and the central unit, with physical control of all plant; the establishment of almost self-contained subcentres attached to large central units associated with university hospitals. Of these, the latter would appear to be the best, for it provides a continuous service locally at main-centre standard.

The usual forms for a central unit are the self-contained cancer hospital providing all services; the radiotherapy institute; and a complete cancer service within the framework of a teaching hospital. The self-contained cancer hospital has the disadvantage that inevitably a great deal of cancer never reaches it, being dealt with by the general hospitals in the course of their ordinary work, and involves duplication of many special departments on a small scale. The separate radiotherapy institute is open to the criticism that it deals in a method of treatment rather than in providing the best treatment for every case. The teaching hospital scheme has much to recommend it,

provided that the cancer department has a distinct organization of its own on which local authorities, and other hospitals are adequately represented. In such a scheme one envisages a radiotherapy block with its own beds, and the surgical cases in the surgical wards of the hospital.

There is another problem which only the Ministry of Health can solve on a national scale, that is the need for provision of nursing facilities for cases beyond active treatment; some could be nursed at home, others need hospitalization. There should be constant medical supervision by doctors having particular experience of this work.

The fact that 45% of the "new cases" attending hospital are advanced suggests that in future "cancer propaganda" should aim at getting patients at an earlier stage of the disease, by education of the public.

Finally, the organization of a comprehensive cancer service will entail the training of a considerable number of workers, medical, technical, statistical and administrative.

Air Commodore Stanford Cade said that in the organization of cancer centres in the future the clinical control should be in the hands of a team and not of one director, be he a surgeon or a radiotherapist. Radiotherapists should be trained to use both radium and X-rays and not X-rays only as was so often the case at present to the detriment of patients. Should a national cancer service be realized, cancer ought to be a notifiable disease, in the same way as tuberculosis. Notification under strictly confidential conditions appeared to him to have many advantages.

Dr. Margaret C. Tod spoke of the clinic system established by the Holt Radium Institute which showed that when clinics were started in outlying districts there was a great increase in the numbers of patients even in rural areas.

Although centralization of treatment was highly desirable it would probably be necessary to establish subcentres. These should be few in number and carefully staffed probably by radiotherapists who would spend part of their time in the main centre.

The Manchester organization had shown that it was possible to get rid of the waiting list if a definite policy of immediate admission of early cases was adopted. Late cases were considered from the point of view of curability and in some purely palliative treatment was given, often without admission.

Much remained to be done before perfect co-operation between all members of the specialist team could be obtained but there were great hopes of genuine improvement.

Dr. Louisa Martindale said that notification would have the effect of reducing the number of patients who came for early diagnosis. If they had a fear that they would be notified they would not come. It was a wrong policy to adopt if it was desired to increase the number of people coming for examination.

Dr. G. W. Blomfield said that the treatment of cancer was, of course, an enormous problem. It was one thing to treat a case, and another thing to give adequate treatment. The ideal was to give the patient the very best and most perfect treatment imaginable. To attain that in every case was absolutely impossible, but they could go far towards it by team work and co-operation. Such team work and co-operation must obtain in diagnosis, in the operative and surgical part of the treatment, and in radiotherapy. He had had a good deal of experience of working with people in all these aspects, and especially along the operative line. He thought that the radiotherapist should be able to do the interstitial radium work as well as the deep X-ray work, and there was no reason why a competent radiologist should not work with the surgeon. But such team work, with the co-operation of all parties, could be obtained only by centralizing the treatment of cancer in the large centres based on the universities. There seemed to be no possibility of obtaining all the necessary personnel without having these large centres. The smaller towns could be covered either by affiliated centres or by some arrangement whereby experts visited the outlying districts. In Sheffield they had a number of outlying clinics. He found that the establishment of an outlying clinic at one of the neighbouring towns resulted in a greater number of cases receiving treatment. The statistics generally bore this out. The underlying necessity was the bringing together of all the experts, the establishment of main centres based on the universities, with subcentres in outlying towns. Dr. Blomfield said that notification might be by serial number, not by name. Neither the patient nor anyone else need be told of the notification.

Professor B. W. Windeyer strongly emphasized the necessity for the complete collaboration of cancer services with other branches of medicine and surgery, both from the point of view of the treatment of the patients and of the training of students.

He did not advocate the segregation of cancer patients except when it was necessitated by the need for specialized treatment and nursing.

He did not consider that the records of cancer patients should be kept separate from general hospital records as it was essential that there should be access to the complete history of each patient for follow-up purposes.

Dr. Charles Wroth thought that the cancer scheme should be considered as part of the rearrangement of medical services now in the melting pot.

All the resources of a consultative out-patient department were needed in the first place. A patient with hemoptysis, hæmatemesis or hæmaturia for example needed specialist investigation, and it looked like being some time before these specialists took kindly to the idea of a "director" unless he had practical experience rivalling their own in all their particular branches. A clinic divorced from these services seemed ineffective.

Mr. A. Dickson Wright said that during the last few weeks he had removed a minute epithelioma from the chin of a doctor and in another doctor a small rodent ulcer from the corner of the eye, and he asked whether these cases were to be notified, and the notification forms to go through the various public offices for all to see. Suppose the medical man used his common sense and did not notify them, would he under the National Health Service incur penalties? The matter bristled with difficulties, the more so because there was a strong feeling among the public that cancer was "catching". For his own part he still felt that all who went to the radiotherapist should be referred to him through a physician or surgeon.

Dr. Malcolm Donaldson said that in the excellent opening to this discussion a memorandum called the ABC Scheme had been mentioned. This memorandum had been written with the idea of making people think, and he believed that if they read it, it would do so. A second objective was to try to get the teaching hospitals and some of the larger voluntary hospitals in the area of London and the Home Counties to come together and to work out some sort of scheme to help the local authorities. He hoped that a meeting might take place at which such a scheme could be drawn up. In the ABC Scheme certain A hospitals would be responsible for the radiotherapy for certain B hospitals where surgery alone was performed. He hoped to see the financial arrangement the same for every class of hospital in the area, so that the local authority would not be biased by one hospital having a cheaper service than another, and practitioner and hospital would have free choice as to which hospital was consulted in the first instance.

Sir Ernest Rock Carling, in reply, referred to his remark that "the profession had got to save itself"; he had in mind the fact that administrative opinion seemed to be hardening on political lines in favour of small administrative authorities. This would not suit medicine and it would not suit cancer treatment or any other form of treatment. They as a profession had to make it perfectly clear to the public that the organization which was wanted was one which covered a large region, because this was the best for health services.

About notification: One of the essentials of the organization of which he had spoken was that every case would be registered at the periphery: If that was done it was the equivalent of notification. Notification at the periphery ought to excite a state of awareness in the whole system. The notifications should arrive at a bureau which would see to it that none escaped, and it was at that bureau that a director would be wanted. The word "director" was often misunderstood. It was not intended that anybody should direct the team what to treat and how to treat it, but that there should be somebody who would correlate all the records, particularly all the registration records, so that no patient escaped from the net and all reached the appropriate member of the team for treatment.

He agreed with what Dr. Nuttall had said about the incurable, but it was part of a large problem—the treatment of the chronic sick. No system of organization amongst hospitals from periphery to centre or centre to periphery would be complete without a well-organized transport system. After the war, bus and train systems, and eventually aeroplanes, would simplify transport. He regarded diagnosis as the function of the outpatient department of a general hospital.

The provision of a hostel in association with a hospital was very important, particularly so in association with diagnostic and treatment centres which cared for ambulant patients. It would be preposterous to use a bed in a general hospital costing £6 a week when the patient could be accommodated in a hostel close by for £2 a week.

He thought it very important that the staff of the associated centres should feel themselves to be a part of the whole area service. In this matter an example had been set by Liverpool University in the pathological service of the Liverpool district of Lancashire. It had resulted in the Professor of Pathology at the University being a welcome guest at every laboratory and in raising the standard of pathology.

One speaker said that he hoped there would not be too much segregation of cancer. A lesson was to be learned from the tuberculosis service. In the tuberculosis service medical superintendents of sanatoria were deploring the fact that they were cut off from communication with the university and the big hospital centres. They knew that they were only a part of "a service for thoracic disease". Of the patients going to the tuberculosis dispensaries only 49% were suffering from tuberculosis. In other words, those in charge of the dispensaries saw a vast number of general medical cases, and so it would be at the preliminary investigation centres of cancer.

Mr. Blomfield had spoken of the necessity for team work in implantation. In some places the surgeon who made the exposure would ask the radiotherapist to implant the seeds, in others the surgeon would be competent to do it himself. He did not think, however, that the general surgeon would be competent to carry out the surgery of access in the anatomical fields of the specialist surgeons.

Mr. Dickson Wright had said that he thought all cases should pass through the hands of a physician or surgeon. That was the view he had held. But, of course, every radiologist before he became such was a physician and surgeon, and many radiologists made an effort to set up a high standard of clinical knowledge.

Dr. Wroth had pointed out that radiotherapy was used for many conditions besides cancer. From some centres the Radium Commission had received reports showing that 50% of the cases treated were in fact not malignant. No doubt an enormous number of dermatological cases would come for treatment, as well as other cases which were said to benefit from radiotherapy, and when there was enough apparatus and an adequate supply of radiotherapists no doubt there would be a larger number of associated centres at which such cases would be received.

It was true that the Ministry and the Radium Commission had asked their centres and other hospitals to supply them with additional records, but the record asked for could be abstracted in nearly every case from the full record the hospital must keep in any event. He agreed that the entire record should be kept together.

Mr. Stebbing, also in reply, said that registration of cancer cases as suggested by the Radium Commission would be more satisfactory than notification to the Medical Officer of Health, the object of registration being to make sure that every suspected case did get actual treatment. If cancer patients were to have satisfactory treatment there must be organization on a bigger basis than the individual hospital—an organization which would spread its net to catch the patient who had an unexplained symptom. Last year there were 1,142 people in Great Britain who died from cancer of the skin, and every radiotherapist knew that if a case of cancer of the skin was taken early it did not die. He doubted whether any of those patients need have died. It was because of all this that there must be a director. Dr. Wroth had suggested that the director should be a radiotherapist. But they were still trying to persuade the surgeons that they had a part to play in the organization of cancer treatment, and in neither of the two pamphlets on this subject was it suggested that the radiotherapist should be a director, unless he had the right kind of experience and personality. It was not a question of the speciality he practised in. The best man of all, perhaps, to be a director would be a pathologist.

All the hospitals—and that meant at the present time the voluntary hospitals, because they had the initiative—should form an organization to serve the districts. This organization should become so well recognized that the local authority would have to make use of it. If the voluntary hospitals waited and did nothing until an organization was imposed upon them from above the situation would be very difficult.

Another speaker had asked how a division was to be made between the labours of the different members of the team. This could be settled in consultation, where they would soon find out who was able to put the needles in best. They must be got into consultation over the case, must see the patient, and discuss the patient, the treatment, and the follow-up. It was very important that the consultation should concern itself with the follow-up as well as with the treatment.

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[November 9, 1944]

An Instrument for Testing Dark Adaptation

By E. W. GODDING

(Research Department, The Crookes Laboratories)

KNOWLEDGE of the phenomenon of dark adaptation is now sufficient to enable the various factors which condition it to be brought under control and to make its evaluation possible. Dark adaptation is defined as the process by which the eye adapts itself to a change in illumination from high to low intensity, the change being accompanied by an increase in the sensitivity of the eye.

The practical measurement of dark adaptation by means of threshold measurements has been found to be dependent on many external physical conditions apart from biological variations in the subjects themselves. It is, therefore, stressed that one of the first requisites for the scientific investigation of the subject is the control of these conditions. Without this, differences in observation and interpretation by different workers are bound to occur. Such control can only be achieved by the standardization of such conditions (*see also* Godding, 1945). This has been attempted and the results applied to the present instrument.

In testing dark adaptation it is necessary to emphasize that we are not testing ability to carry out actual visual tasks at night (described by Livingston as "night visual capacity", 1942). In the first case we are concerned with the evaluation of the phenomenon of dark adaptation itself, in the second with the unlimited number of special tests which can be elaborated in respect of particular visual tasks, e.g. night flying. Night visual capacity may be described as the individual response resulting from all the factors concerned in the particular task, visual, adaptive, psychological and training; in other words, the reactions of the subject as a whole. Good dark adaptation is an obvious requirement for a high standard of night visual capacity, but no other correlation exists.

It follows that an instrument designed to test dark adaptation is ideally one which, when used to evaluate this process, does not evaluate anything else, and a patch of light, suitably controlled, is, in theory, the most suitable means for testing dark adaptation.

There are, however, a number of complicating factors. For example, as is well known, different areas of the peripheral retina of the dark-adapted eye are not equally sensitive; the most sensitive area being an annulus between some 10° and 20° around the fovea. This varying retinal sensitivity has given rise to sharp differences in the methods of testing dark adaptation. Hecht and Schlaer (1938), for example, insist on the necessity of testing a definitely located retinal area (obviously requiring a fixation spot), whereas many workers in this country—Yudkin, Wilkinson, Pollak and others—have used a test object without a fixation spot. Since under the stimulus of light the eye automatically tends to use the most sensitive part of the retina, a lack of uniform sensitivity does not necessarily require the testing of a definite retinal area.

If a test object is used, it should make the minimum demands in regard to acuity, and its shape should be such that recognition is automatic. It has been found (Craik and Vernon, 1942) that the results obtained by the use of such a test object are parallel with those obtained by the use of a patch of light only, and experience has shown that the

results obtainable by the use of a test object without fixation are at least as reproducible as those obtainable by the use of light flashes accurately located.

Irrespective of the method used, what is aimed at in an instrument is one which gives results in absolute units of illumination or brightness, results reproducible on the same instrument, and from instrument to instrument. The steps taken to achieve this are described along with the following general description of the apparatus.

Electrical Circuit

A voltage stabilizer produces a steady output from any input voltage between 190 and 260 volts A.C. (Frequency must be 50 cycles.) The apparatus can, therefore, be used without modification with most of the electric supply services throughout the country. A 12 volt circuit incorporates the "bleaching" lamps and a 4 volt circuit the test lamp. Variable resistances are used but only as a means of providing final fine adjustments to standard brightnesses.

The Bleaching or Light-Adapting Apparatus

For the normal healthy person, Craik and Vernon (1941a) have shown that the time taken to become dark adapted depends largely upon the intensity of light to which the eye has previously been exposed: from low intensities (100 to 200 ml.) dark adaptation is almost complete in ten to fifteen minutes; from moderate intensities (500 to 1,000 ml.) adaptation is largely completed in twenty to thirty minutes, and with high intensities (10,000 ml. for example) the process is further delayed. In the testing of dark adaptation, therefore, a standard pre-treatment of the subject is necessary by the standardization of the previous light or "bleaching" exposure. The intensity should be sufficiently high to ensure that subsequent dark adaptation is not so rapid as to make its evaluation difficult, and to make evident the transition from cone to rod vision. (Shown as a "kink" in the dark adaptation curve, see figs. 2, 3 and 4.)

The brightness of the bowl is 750 ml. which viewed for five minutes meets the above requirements and also conforms to the standards now adopted by Craik (personal communication). This brightness can be viewed by the great majority of subjects without discomfort and is not so high as to give rise to complications due to after-images (Craik and Vernon, 1941b). The colour temperature at 750 ml. is approximately 2,750°K.

If the subject has been exposed for any appreciable period to a high brightness before this light adaptation is commenced, as may happen on any sunny day, the subject should be put in an internally lit room for about half an hour, with all light sources shielded. Even this added precaution will not neutralize the effects of prolonged previous exposure to very high brightnesses. This use of internal illumination should not be replaced by darkness since it has been shown (unpublished data) that immediate preliminary dark adaptation has an accelerating effect which is particularly marked in the case of subjects whose curves show subnormal recovery times. Thus the diagnostic value of the test tends to be lost. This effect, as might be expected, is maximal at the higher intensities, tending to disappear towards the final threshold. It follows that intervals should always be allowed between repeated tests on the same individual.

As one method of testing is by means of a test object without fixation it is necessary to bleach evenly the whole of the retina. With the subject's head in the correct position (i.e. the eyes as near as possible to the bowl) the pupils are almost at right angles to the edge of the concave bleaching surface. The even bleaching of the extreme retinal periphery can be obtained by a rotation of the eyes. An even brightness of the bleaching surface (excepting the slightly lower brightness of the extreme edge) has been achieved.

The Test Light Unit

As is well known, the eye is not equally sensitive to all parts of the visual spectrum. Further, whereas the light-adapted eye is most sensitive to a wavelength of about 560 mμ, the dark-adapted eye is most sensitive to a wavelength of about 510 mμ. Hecht and Shlaer use a violet filter to obtain the maximum range of rod values. It is clearly necessary that full particulars of the spectral values of the test light used must be given. In this instrument white light is used for the standard test and the colour temperature of the test field is approximately 2,500°K.

A means of accurately varying the brightness of the test field or object over a considerable range must be provided. Various methods of reducing the intensity have been used, e.g. rheostats, neutral density filters and wedges, polarizing discs, diaphragms, and so on, but the use of a rheostat is unsound since marked changes are introduced in the spectral values of the light. The method used in this instrument is to keep the source of illumination constant and to reduce the brightness to 1/10th, 1/100th, 1/1000th, &c., by means of neutral density filters and to achieve intermediate stages by the use of

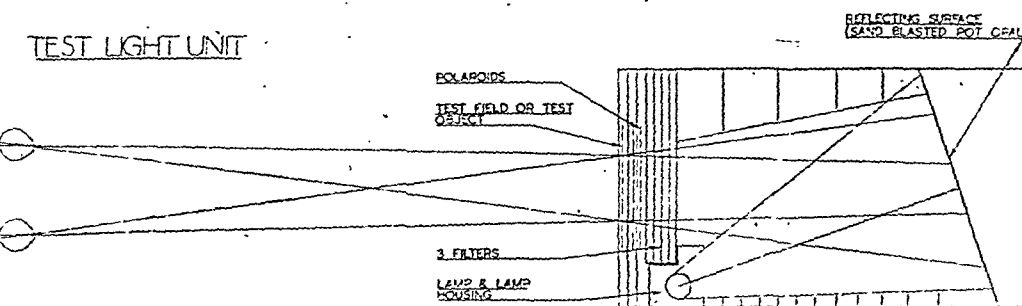


FIG. 1.

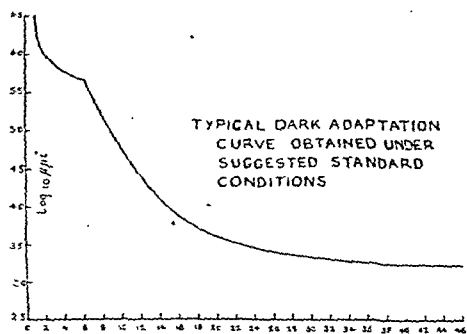


FIG. 2.

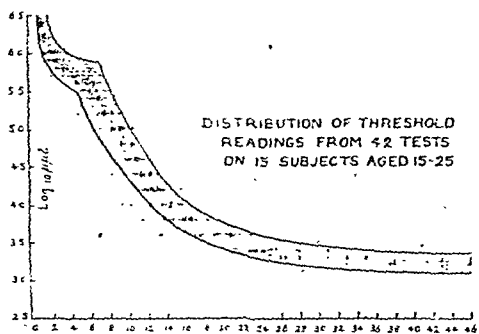


FIG. 4.

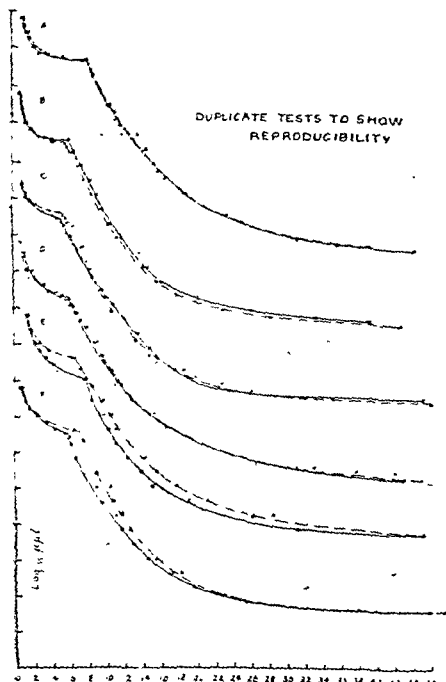


FIG. 3a.

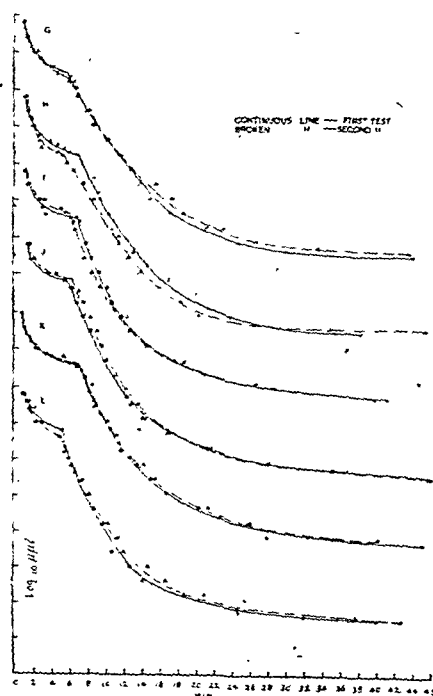


FIG. 3b.

From the lowest duplicate pair of curves upwards each successive pair is displaced 1 log unit.]

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A means of accurately varying the brightness of the test field or object over a considerable range must be provided. Various methods of reducing the intensity have been used, e.g. rheostats, neutral density filters and wedges, polarizing discs, diaphragms, and so on, but the use of a rheostat is unsound since marked changes are introduced in the spectral values of the light. The method used in this instrument is to keep the source of illumination constant and to reduce the brightness to 1/10th, 1/100th, 1/1000th, &c., by means of neutral density filters and to achieve intermediate stages by the use of

less than 0.2 sec., since the stimulus effect of shorter exposures depends on both the duration of the flash and the intensity, but for exposures of 0.2 sec.; and over, the stimulus effect is proportional to intensity only. This fact should be used only in the testing of a definitely located retinal area. Where a test object without a fixation spot is being used, longer exposures than 0.2 sec. are certainly required to obtain correct threshold values. Grindley (1931) shows that at least 1 sec. is necessary to obtain lowest threshold readings at higher intensities, and experience has shown that at the lowest intensities exposures up to 1 min. or more are required. The usual procedure when using a test object without fixation is to use a constant light source.

The exposure unit for obtaining light flashes is described later under "Alternative Method of Testing".

The limitations on the distance at which the test should be carried out are not clear. No data exist for rod vision which show at what minimum distance there will be no pupil contraction reflex effect, due to fixational distance stimulus. At higher intensities (0.1 ml.), Luckiesh and Moss (1937) have shown that the size of the pupil, although smaller for binocular vision than for monocular, is not altered significantly by any increase in distance over 2 ft., and it is suggested that this may be regarded provisionally as the minimum distance for adoption as standard. The test is, therefore, carried out at a distance of 2 ft., and at this distance the diameter of the test object—an arrow—subtends a visual angle of 7 degrees. Regarding the shape of the arrow, the aim has been to design this so that no part of it is seen as such before its shape is appreciated as a whole. The arrow can be rotated to point in any one of four directions, thus providing a check on the responses of the subject.

Artificial pupils for subjects with healthy pupillary reflexes would appear unnecessary, for routine testing, providing the distance requirement is met. If it is desired to correlate findings with those of workers using an artificial pupil, Mandelbaum (1941a) has supplied a correction factor which enables this to be done; the use of a miotic and measurement of the pupil diameter are of course necessary.

The test can be carried out either monocularly or binocularly.—Most workers have found, as would be expected, that the final threshold reached is lower for binocular vision than for monocular vision. Psychological errors are perhaps more likely to be avoided by the use of both eyes, since a monocular test does introduce for some subjects a somewhat unusual element. A binocular test is recommended for routine testing as standard for this instrument.

Regarding acuity and the wearing of glasses, small and medium errors of refraction, as would be expected, appear to have little effect on threshold readings when flashes of light or relatively large, simple test objects are used. It is recommended that vision under 6/18 should always be corrected for the test. The loss of light by reflection and absorption of lenses is approximately 10%. The effect of this on threshold values is relatively small (approximately 0.5 log unit) but should be noted.

Fusion would appear to be a necessity in order to obtain the lower binocular threshold over the monocular, but Pirenne's (1943) latest work has cast some doubt on the matter.

Absolute Standardization

(1) "*Bleaching*" light.—Visual photometry is used to establish a brightness of 750 ml. obtained by means of a variable resistance control. The colour temperature at this brightness in different instruments will be subject only to small differences.

(2) *Test light*.—The ideal is that the brightness value at any "step" throughout the range covered shall be accurate. The chief difficulty in standardization by means of visual photometry is due to the inability of the eye to make accurate brightness difference estimations at very low brightnesses, and also to the shift in spectral sensitivity towards the blue end of the spectrum for the dark-adapted eye. This means that any attempt to carry out direct measurements at the lowest brightnesses concerned must be subject to gross errors, and with any light source which is not "neutral" different values will be obtained at higher and lower brightnesses. Difficulties of a somewhat similar nature appear when using photo-electric methods.

In the case of the present instrument the filters and the polaroid discs approximate closely to neutrality and thus with white light of constant spectral values the second difficulty does not appear. As to the difficulty in carrying out direct measurements at the lower intensities a practical solution is to measure the components singly and to establish a relationship for their combined use; alternatively to measure the whole unit at higher brightness levels and to obtain the required values by inference.

The first method has been used, and the following characteristics established by the National Physical Laboratories:

- (1) The transmission of the polaroid discs and their conformity to Cos^2 Law within the angles of crossing as used in the instrument.
- (2) The transmission of the neutral density filters. Owing to different methods of standardizing filters it is essential that the standardization should be carried out under the conditions of use. The filters were required to be of 1/10th and 1/100th transmissions within close limits. These values were established.

polaroid discs, one fixed and the other rotatable.¹ The lamp illuminates the sand-blasted pot opal glass screen which is placed normal to the lamp (fig. 1). The observer views this surface at a distance through the polaroid discs and neutral density filters as required. The variation in brightness of the different parts of the reflecting surface depends on the relative distances from the lamp and the angles involved. When compared with a point at the centre, a point at the extreme edge of the portion of the reflecting surface used theoretically will be less bright by about 8%. When a point of the arrow is viewed binocularly under the conditions of the test, however, this difference is largely compensated since the two fields of view of the reflecting screen are not identical, the point of least brightness for the L.E., for example, corresponding to a point of higher brightness for the R.E. As the subjective brightness sensation will be the integrated effect of the two brightnesses, this clearly will lessen the theoretical difference.

The reflecting screen is viewed by the observer at an angle of approximately 12 degrees from the normal. With diffuse light this will not affect the brightness of the projected field. The photometric standardization is carried out under the same conditions.

It should be noted that different thicknesses of sand-blasted pot opal, when suitably backed, give almost identical reflection factors, so that in contrast to the variability of pot opal when used as a transmitting medium, a considerable gain in reproducibility and ease in replacement is achieved.

The limiting light screens have been introduced in order to reduce the effects of reflection from the internal walls to a negligible quantity, thus the effect of any deterioration in the interior surface of the unit will also be negligible.

Polaroids and Neutral Density Filters

The filters are: one neutral density filter transmission 1/10th (density 1), and two neutral density filters transmission 1/100th (density 2).² The polaroids decrease the brightness smoothly and are used to provide a 10:1 range only. The scale attached to the rotating polaroid is graduated in steps of .05 log unit (approximately 10%) so that the polaroids together with the filters provide a means of decreasing the brightness by a million to one in steps of .05 log units.

The highest brightness obtainable, that is with the polaroids only, the rotatable polaroid being at Mark 0 on the scale, is 0.4 ml., or 400,000,000 micro micro lamberts, and the lowest brightness, with the polaroids and all the filters in position, is .0000004 ml. or 400 micro micro lamberts. To reduce these figures to convenient proportions, the logarithm of the number is used so that since the logarithm to base 10 of 400,000,000 is 8.6, and of 400 2.6, the ratio is 6:1 in log units which is, of course, the same thing as a million to one. It should be noted that a logarithmic scale is attractive for other reasons. As Mandelbaum says: "Each log unit indicates a tenfold change which is directly applicable in a physiological sense as indicating the regeneration of a definite percentage of visual purple and reflects the course of adaptation in the human eye."

The bleaching and test light units will again be referred to under Absolute Standardization.

The Size of Test Object or Test Field, Exposure Time, and Distance for the Test

In attempting to further the establishment of standard conditions, which is the chief purpose of this paper, it is obviously desirable to eliminate, whenever possible, factors which in themselves can affect the threshold measurements. It would appear that all the factors under the present heading can be eliminated as conditioning factors, provided certain requirements are met.

As the size of the test object or field increases, the threshold values decrease until a limit is reached when the stimulus effect is proportional to brightness only. With objects subtending 7 degrees, threshold brightness appears to be almost independent of area considerations (Piper, 1903; Lohle, 1929). This is in general agreement with the work of Graham, Brown and Mote (1939). Hecht (1937), however, was able to produce equally low threshold values with a test field subtending only 2 degrees by carefully locating this on the most sensitive part of the peripheral retina. It is recommended, therefore, that unless the test field or object is fixated as described by Hecht the visual angle subtended should be at least 7 degrees.

In regard to exposure times, the Bunsen-Roscoe (Blondel-Rey) law indicates that if flashes of light are used for the dark adaptation test, then the exposures should be not

¹Hallimond (1944) has recently investigated the physical properties of the new H polaroid, the material used, and his results fully confirm its suitability for the purpose described.

²The density figure is the logarithm of the reciprocal of the transmission, e.g. Transmission 1/100, expressed as density = Log. 100 = 2.

Any attempt to test dark adaptation by taking single readings at shorter dark-adaptation times has been shown to be subject to gross errors. Since the sensitivity of the eye is rapidly changing for the first ten to fifteen minutes, such errors appear inescapable under the conditions which must apply to routine testing and it is clear that the nature of the phenomenon precludes the use of short simple tests.

Perimetry at Low Intensities

A special use for the instrument should be mentioned. Sloan (1939), Mandelbaum (1941b), and more recently Livingston (1944) have all described methods of taking perimetric measurements with the dark-adapted eye. It would seem that the present instrument, with little modification, might be used for taking such measurements.

Normal Response Data, Obtained by the Use of a Test Object Without Fixation

For the successful application of the test the first essential is that any particular instrument should give reproducible results. Reproducibility can be determined with reasonable accuracy by carrying out repeated tests at short intervals on one or more subjects, but such results, almost inevitably, will include biological variations, in addition to errors due to the limitations of the apparatus and the technique used.

For this purpose twelve subjects (six male and six female) were tested and retested within a few days (figs. 3a and 3b).¹

In nine of these duplicate tests the results are almost identical, in two (E, F) the second test is not so good as the first, and in one (H) the second test is the better of the two. Taken as a whole and bearing in mind the highly probable inclusion of some variation due to biological causes, it is suggested that these results provide satisfactory evidence of the reproducibility of the test.

The chief requirement is to establish a normal range of responses, preferably for different age-groups, among subjects who are clinically healthy and in a satisfactory state of nutrition. This has proved difficult of attainment during wartime, but a start has been made on an age-group of 15 to 25 and undesirable material eliminated as far as possible by means of a preliminary ocular examination and general questionnaire.

Twelve medical students and eight nurses volunteered for the test. From these, four were rejected as follows:

- One with uncorrected defective vision (L/E 6/60).
- One with history of nervous debility and unsatisfactory diet.
- One with history of chronic sinusitis and frequent colds.
- One with history of tuberculous glands and unsatisfactory diet.

No attempt was made to give vitamin supplements before testing.

Fig. 4 shows the distribution of threshold readings from forty-two tests on fifteen of these subjects (nine male and six female). As no correction has been made for pupil size, the effect of differences between individuals is included in the results. The few readings above the apparent normal range are random readings from a number of tests, but those below it are from two tests on the remaining subject in the group. Additional data are clearly required before deciding whether such outstanding adaptation should be regarded as coming within the normal range.

In conclusion it is obvious that a universally accepted test and technique for the testing of dark adaptation would be an immense advantage from the point of view of the correlation of results, and it is emphasized that the adoption of standard conditions for the method used is the important matter irrespective of the actual form of this or any other apparatus.

Space does not permit me to thank all those who have generously collaborated in the development of the adaptometer, but special thanks are due to Dr. Kenneth Craik and Dr. J. W. T. Walsh. I am indebted to the Administrative Staff, students and nurses of the Central Middlesex Hospital for the facilities which enabled me to carry out the tests.

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¹ Two of these duplicate tests (A and J) were on subjects who were rejected from the normal group. Their adaptation though not good was reproducible.

- (3) The transmission for the polaroids and one filter combined, and also for all the filters in combination, the latter value being obtained at a level representing the dark-adapted eye but at an intensity which enables reasonable accuracy to be obtained. The results confirmed that the combined use of the polaroids and filters produced the theoretical transmissions within close limits.

With the above characteristics established the routine standardization of the instruments is carried out as follows:

- (1) Selection of neutral density filters which conform to standard 1/10th and 1/100th filters.
- (2) A lamp which has been aged and standardized for H.C.P. is placed at such a distance from the reflecting surface as to produce a "standard" brightness of the screen: The polaroids are placed in "parallel" and the variable resistance adjusted so that the brightness of the screen is brought to a standard. The voltage required then becomes standard for the instrument. Finally the transmission of the polaroids is confirmed for various angles of crossing.

By bringing all instruments to the same brightness level (with the polaroids in position) and using selected filters of 1/10th and 1/100th transmissions it is possible to construct a standard log scale for the rotating polaroid. This in turn enables a standard form and graph paper to be used, thus simplifying considerably the task of plotting data.

For replacement purposes the following routine estimations are also carried out: reflection factor of the reflection surface, and transmission of the polaroids, singly and in parallel.

To Carry Out the Test

(a) *With a test object and no fixation spot.*—The subject is seated comfortably and the facepiece of the instrument brought into position by adjustment of the stand. The extension piece is then replaced and the instrument pivoted so as to bring the "bleaching" apparatus in line with the subject, who is then instructed to lean forward with the eyes as close to the glass bowl as possible. Both bleaching light and test light are switched on (this stabilizes the test light before the test commences) and the subject looks into the bowl as previously described, for five minutes. At the end of this time the "bleaching" light is switched off, the subject instructed to sit back, the instrument rotated as before and the facepiece again extended. The voltage for the test light is adjusted to the standard voltage for the instrument, the first neutral density filter 1/100th brought into position and the polaroid scale put at mark 0. This gives a brightness of $10^{6.6}$ micro micro lamberts (or 6.6 log units), which will be seen at approximately half a minute.

As soon as the arrow is seen the time is noted and the brightness immediately decreased by means of the rotating polaroid. The time taken to see this lower brightness is again noted and so on, the position of the arrow being continually varied. The neutral filters are successively introduced until in combination with the polaroids the "final" threshold reading at thirty to forty-five minutes is taken. The readings are confirmed towards the end of the test.

For the last fifteen to twenty minutes of the test the subject should be instructed to close the eyes between readings as far as possible. At any time when fatigue is complained of the subject should be so rested. This is more important than taking every possible reading. It is emphasized that attempts to obtain rapid readings at the lowest brightnesses, when a fixation spot is not being used can only result in considerable errors.

The plotting of the data obtained as a curve on the special graph paper supplied is carried out easily and quickly (fig. 2).

(b) *Alternative method of testing—light flashes.*—The test object is removed and the separate exposure unit placed in position. The device consists of a pendulum disc with a central opening. This pendulum swings across the test field aperture and is held either to the left or right by means of a magnetic coil. An exposure is made, therefore, by the swinging of the pendulum in either direction, a simple switch action controlling the movement. The size of test field, its location, and the duration of the flash, can be varied. The conditions as adopted by Hecht and Schlaer and other American workers are a test field subtending 2 degrees fixated 7 degrees peripherally, and the exposure time approximately 1/5th sec. The red fixation light is of variable intensity with no wavelength shorter than 6,200 Å. The facepiece and chin rests are adjustable and provide for both monocular and binocular testing.

If used, a monochromatic filter is introduced. The test is carried out in a similar manner to that described for the use of a test object except that as described by Hecht and Schlaer it is usual to find the intensity which can be seen at fixed intervals instead of the time taken to see predetermined brightnesses; also with this instrument the whole of the retina is bleached as previously and not a part only. If desired to follow the Hecht-Schlaer technique precisely then it would be a simple matter to provide a mask and fixation spot to accomplish this.

Simplification of the test.—For certain purposes a simplification of the test is justified, the usual procedure being to determine the lowest intensity of light which a fully or almost fully adapted subject can see, usually at thirty to forty minutes dark-adaptation time. The soundness of the procedure is further supported by the work of Hunt and Palmer (1940) who have shown (using light flashes only) that the mean deviation at thirty minutes adaptation is less than at any previous dark-adaptation time. Unfortunately, the "final" rod threshold is not always a true indication of the whole course of adaptation (Craik and Vernon, 1942). Yudin (1943) and others have shown, however, that this measurement is of particular value for certain purposes but full curves are essential when information is required regarding recovery times and threshold values at higher intensities.

Any attempt to test dark adaptation by taking single readings at shorter dark-adaptation times has been shown to be subject to gross errors. Since the sensitivity of the eye is rapidly changing for the first ten to fifteen minutes, such errors appear inescapable under the conditions which must apply to routine testing and it is clear that the nature of the phenomenon precludes the use of short simple tests.

Perimetry at Low Intensities

A special use for the instrument should be mentioned. Sloan (1939), Mandelbaum (1941b), and more recently Livingston (1944) have all described methods of taking perimetric measurements with the dark-adapted eye. It would seem that the present instrument, with little modification, might be used for taking such measurements.

Normal Response Data, Obtained by the Use of a Test Object Without Fixation

For the successful application of the test the first essential is that any particular instrument should give reproducible results. Reproducibility can be determined with reasonable accuracy by carrying out repeated tests at short intervals on one or more subjects, but such results, almost inevitably, will include biological variations, in addition to errors due to the limitations of the apparatus and the technique used.

For this purpose twelve subjects (six male and six female) were tested and retested within a few days (figs. 3a and 3b).¹

In nine of these duplicate tests the results are almost identical, in two (E, F) the second test is not so good as the first, and in one (H) the second test is the better of the two. Taken as a whole and bearing in mind the highly probable inclusion of some variation due to biological causes, it is suggested that these results provide satisfactory evidence of the reproducibility of the test.

The chief requirement is to establish a normal range of responses, preferably for different age-groups, among subjects who are clinically healthy and in a satisfactory state of nutrition. This has proved difficult of attainment during wartime, but a start has been made on an age-group of 15 to 25 and undesirable material eliminated as far as possible by means of a preliminary ocular examination and general questionnaire.

Twelve medical students and eight nurses volunteered for the test. From these, four were rejected as follows:

- One with uncorrected defective vision (L/E 6/60).
- One with history of nervous debility and unsatisfactory diet.
- One with history of chronic sinusitis and frequent colds.
- One with history of tuberculous glands and unsatisfactory diet.

No attempt was made to give vitamin supplements before testing.

Fig. 4 shows the distribution of threshold readings from forty-two tests on fifteen of these subjects (nine male and six female). As no correction has been made for pupil size, the effect of differences between individuals is included in the results. The few readings above the apparent normal range are random readings from a number of tests, but those below it are from two tests on the remaining subject in the group. Additional data are clearly required before deciding whether such outstanding adaptation should be regarded as coming within the normal range.

In conclusion it is obvious that a universally accepted test and technique for the testing of dark adaptation would be an immense advantage from the point of view of the correlation of results, and it is emphasized that the adoption of standard conditions for the method used is the important matter irrespective of the actual form of this or any other apparatus.

Space does not permit me to thank all those who have generously collaborated in the development of the adaptometer, but special thanks are due to Dr. Kenneth Craik and Dr. J. W. T. Walsh. I am indebted to the Administrative Staff, students and nurses of the Central Middlesex Hospital for the facilities which enabled me to carry out the tests.

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Studies in Dark Adaptation in the Detection of Deficiency of Vitamin A

By Captain JOHN YUDKIN, M.A., Ph.D., M.D.(Cantab), F.R.I.C., R.A.M.C.

THAT studies in dark adaptation may be utilized to detect deficiency of vitamin A depends on three observations (*see* Yudkin, 1944a). First, individuals known to be living on diets deficient in vitamin A show poor dark adaptation. Second, experimental deprivation of the vitamin leads to impairment of dark adaptation. Third, administration of vitamin A to individuals with poor dark adaptation often leads to its improvement.

The investigations to be described were all carried out with the earlier Crookes' apparatus, described by Haines, 1938 (*see also* Yudkin, 1941a), and modified in certain respects by G. W. Robertson and myself (Yudkin *et al.*, 1943; Robertson and Yudkin, 1944a).

Before undertaking studies of dark adaptation in nutritional surveys certain questions had to be answered. Since it is impracticable to determine the complete course of dark adaptation for large numbers of subjects, would the measurement of one threshold at a certain time after the beginning of adaptation provide a satisfactory index of the general dark adaptation power of the subject? If so, which stage provides the best index both of degree of adaptation and of possible vitamin-A deficiency?

The course of dark adaptation.—These questions were answered by a study of the complete course of dark adaptation in about 400 subjects and by observations of the effects of vitamin A in many of these (Yudkin *et al.*, 1943).

The first fact which emerged was that, if only one point in the dark-adaptation curve was measured, the relative performance of different individuals might differ considerably, depending on whether this one point was early or late in the course of adaptation. The change in the relative performance of the subjects may occur up to about twenty minutes of dark adaptation.

From these considerations alone, therefore, it seemed that if the measurement of dark adaptation is to be made in survey work, the final rod threshold is probably the best.

Effect of vitamin A on the course of dark adaptation.—It was found that, if vitamin A produced any significant change in the curve, there was always a change in the final rod threshold. Allowing for the fact that the rod threshold is always affected by vitamin A, then there are four possible changes which might be induced by vitamin A.

- (1) Change in final rod threshold only.
- (2) Change in final rod threshold and cone threshold.
- (3) Change in final rod threshold and cone-rod transition time.
- (4) Change in final rod threshold, cone threshold and cone-rod transition time.

Each one of these types has been observed among our subjects.

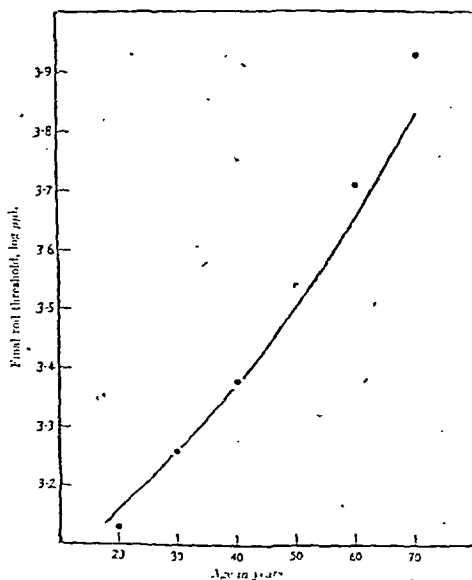
From the point of view of detecting deficiency of vitamin A, therefore, the one single point in the course of dark adaptation which would be expected always to show a change is the final rod threshold. Consequently, this was the measurement always made as a routine when carrying out survey work.

Measurement of dark adaptation in nutrition survey.—It is necessary here to emphasize that measurement of the final rod threshold in an individual cannot alone be taken as an index of sufficiency or deficiency of vitamin A. Earlier workers believed that there was a narrow normal range of dark adaptation and that values of visual threshold above this range could be taken as presumptive evidence of deficiency of vitamin A. It became apparent, however, that the "normal", or rather average, range of dark adaptation was fairly wide. For example, the range of final rod threshold was more than ten times or one log unit. In other words, the normal range adopted by the earlier workers excluded some individuals with no deficiency of vitamin A and included some with such deficiency. As a result, workers have recently tended more to use the therapeutic test and to take as the criterion of deficiency the improvement of dark adaptation following administration of the vitamin (Yudkin, 1941b; Steven and Wald, 1941).

Nevertheless, it seems possible to adduce at least presumptive evidence of deficiency of vitamin A in groups of individuals without the necessity for determining the vitamin-A lability of their dark adaptation. If there is a significant difference in the average values of dark adaptation in two strictly similar groups, it seems legitimate to conclude that the group with the inferior dark adaptation is, on the whole, probably at a lower level of vitamin-A nutrition, provided there is no reason to suspect other causes for the difference. Most of these causes are pathological and fairly readily recognized; they include, for example, ocular causes such as retinitis pigmentosa, and metabolic causes, such as hepatic cirrhosis. An important physiological cause of differences in dark adaptation is age.

Dark adaptation and age.—A group of 758 factory workers, whose age ranged from 14 to 70 years, provided us with material for a study of this question (Robertson and Yudkin, 1944a). The results showed that there is an increasing deterioration of dark adaptation with age. Between 20 and 30 years the increase is about 0.10 log units and between 50 and 60 years it is about 0.15 log units. The correlation coefficient of age and increasing final threshold is 0.56.

There are various possible reasons for this deterioration of dark adaptation with age: decreased transparency of the ocular media, decreased sensitivity of the retina, diminished size of the pupil, &c. We have found, however, that one of these, the progressive decrease in size of the dark-adapted pupil, is sufficient to account quantitatively for the deterioration with age which we have measured. Figures have been published for the average size of the dark-adapted pupil at different ages. If we calculate from these figures the effect of decreasing pupil size in decreasing the amount of light reaching the retina and hence the required increase in the threshold necessary to get the same visual effect, we find that the calculated threshold at different ages agrees very well with those found (fig. 1).



Continuous line: observed variation.
Points: "expected" variation, calculated from change in pupil size.

FIG. 1.—"Expected" variation of dark adaptation with age due to diminution of pupil size with age. (From *J. Physiol.*, 1944, 103, 6.)

It seems possible, therefore, to determine the probable relative status of different groups in regard to vitamin A by measuring their dark adaptation, provided there is present in none of the groups a pathological condition other than dietary deficiency which might affect their adaptation and provided that the groups are of similar age or that allowance is made for the difference in age. There is, however, evidence that exceptions may exist to each of the three criteria enumerated above. It is possible also that large doses of vitamin A may produce a "super-normal" dark adaptation and we may be dealing with pharmacological action rather than replacement therapy. In view of these findings, therefore, evidence of poor dark adaptation alone, such as we have suggested might be

obtained for the comparison of the vitamin A status of different groups, must be accepted as a less certain criterion than if it is combined with evidence of improvement following administration of the vitamin.

Comparison of Dark Adaptation in Various Groups

Because of the effect of age on dark adaptation, we have divided our subjects into three age-groups; first, school children between 9 and 12 years; second, young adults between 15 and 22, and third, older subjects over 22 (Robertson and Yudkin, 1944b).

School children.—Children from four schools were examined. The first was a senior school in a fairly well-to-do part of Cambridge (Yudkin, 1944b), the second a junior school in one of the poorest areas of Cambridge, the third a Cambridge home for waifs and strays where the dietary practice was of a high standard, and the fourth a village school a few miles from Cambridge. The values for dark adaptation for the three town schools showed no significant difference, whilst those in the village school, where the diet might have been expected to be better than at least the second of the town schools, were significantly lower.

Young adults.—These comprised 346 young Birmingham factory workers (out of a total of 758), 100 Cambridge medical students, 95 students from one of the Cambridge Women's Colleges, 53 younger nurses from Addenbrooke's Hospital (of a total of 126 nurses) and 28 workers from a Sheffield steel factory (of a total of 60 workers). The results show that the dark adaptation of the nurses and of both groups of students was equally good and was better than that of the Birmingham and Sheffield factory workers.

Older subjects.—The values for these older subjects have been compared with the average values at different ages of the Birmingham factory workers, the largest group studied. The 32 older Sheffield factory workers gave values similar to the Birmingham workers, 16 being better and 16 worse than the Birmingham average. The 73 older nurses gave values slightly superior to those of the Birmingham workers, 43 being better and 30 worse. The relative dark adaptation of these groups is the same both for subjects less than 22 years and those more than 22.

Effect of Vitamin A in Various Groups

Vitamin A given to half of the children in each of the three town schools effected no change in their dark adaptation, a fact consistent with their apparently good dark adaptation. It was unfortunately not possible to determine the effect of vitamin A in the children from the village school.

Some of the Birmingham factory workers were also given vitamin A, together with vitamins B, C and D, in pellets which were to be taken daily for a year. The dark adaptation of 178 of the controls showed no appreciable change (improvement of 0.002 log units), whilst the 147 workers who claimed to have taken the pellets regularly showed a significant improvement of an average of 0.073 log units. Of the controls, 58 improved, 71 were unchanged (i.e. changed less than 0.2 log units), and 49 deteriorated; of the vitamin group, 73 improved, 46 were unchanged, and 28 deteriorated. Again, the difference between the two groups is statistically significant.

SUMMARY

(1) If vitamin A affects any part of the dark-adaptation curve, it always affects the final rod threshold; other parts of the curve may or may not be affected. It follows that if only one point in the curve is to be measured it should be the final rod threshold.

(2) In order to prove the existence of vitamin-A deficiency by measuring dark adaptation, it is necessary to apply the therapeutic test, that is, to see whether the dark adaptation is improved after administration of the vitamin.

(3) Although the therapeutic test is essential in order to detect deficiency in an individual and desirable in groups, it is not always practicable to apply it to groups. In this case, presumptive evidence of deficiency may be obtained by comparing the dark adaptation of different groups.

(4) Since age affects dark adaptation, it is necessary either to allow for this in comparing groups of different ages or to compare groups of similar age.

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Dr. H. Pollak reported four cases and presented observations suggesting that dietary factors other than vitamin A may influence dark adaptation. The instrument used was the Crookes' adaptometer [1]; the technique of measurement has been described elsewhere [2]. Significant improvement in the rate and extent of dark adaptation was seen in peptic ulcer patients following injections of crude liver extract and also with brewer's yeast. With regard to injections of liver extract a non-specific, "protein" effect [3, 4, 5] may play a part. A significant speed-up of dark adaptation was also seen following auto-hemotherapy (Case III) which treatment may be regarded as a mild form of "protein" therapy [6]. Systemic effects produced in this way were in man demonstrated by Scarborough [7] who found a striking increase in capillary resistance following reinjection into the tissues of small amounts of patients' own blood.

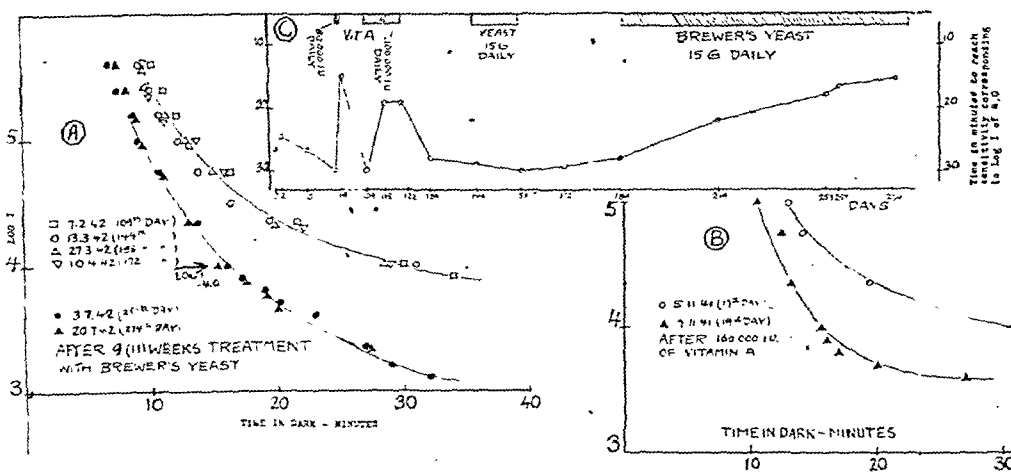


FIG. 1.—Showing changes in dark adaptation. (A) following treatment with brewer's yeast; (B) during and after treatment with vitamin A; (C) changes in dark adaptation on repeated tests over a period of 274 days, recorded by plotting the time required in the dark to reach a threshold of 4.0 log units.

CASE IV (fig. 1).—Man aged 40. Duodenal ulcer. Repeated tests during the first four months of observation showed, apart from temporary responses to large doses of vitamin A by mouth, no tendency to improvement (empty symbols). After prolonged treatment with brewer's yeast, his dark adaptation was finally restored to normal.

Prolonged treatment with yeast seems necessary to produce an effect, no improvement having been seen in any case under six weeks. Significant changes in dark adaptation were also recorded in a case of so-called Plummer-Vinson syndrome during treatment with riboflavin injections and after prolonged treatment with brewer's yeast.

The observations reported here and elsewhere [2] suggest that sources of vitamin-B complex such as certain crude liver extracts and brewer's yeast may, in some cases, influence dark adaptation. Something else besides vitamin A contained in raw liver, which has since ancient times been recommended for the cure of nightblindness, may in part be responsible for this effect.

It is pointed out that a therapeutic response to vitamin A (and for that matter to any other dietary factor) does not necessarily indicate a lack of that particular factor in the diet; the fault may, more often perhaps, lie, even in apparently healthy subjects, in some metabolic inefficiency, the relation of which to dietary factors may be presumed to be indirect and complex. It is of interest here to note that Sullivan and Evans [8] have recently found in the rat that the susceptibility to vitamin-A deficiency depended on the nutritional level of vitamin-B complex and the quality of fat, and interrelationships with other dietary factors are beginning to be recognized.

(Abstract).

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Major R. E. Wright: Few ophthalmologists in this country have had an opportunity of seeing predominant "A" deficiency in a markedly affected population. Having lived in the midst of such a population I would emphasize the importance of viewing the problem of defective metabolism from the clinical angle.

I shall illustrate my point by a few brief examples. The first concerns defective night vision. In Southern India where predominant "A" deficiency is rife, where kera-

tomalacia constitutes a great cause of preventable blindness, and where large numbers of the population are on the verge of clinical manifestations of vitamin-A deficiency, defective night vision is not really a great problem. In some cases one may have obvious signs of "A" deficiency without night vision being inconvenienced. If we select the disturbances of dark adaptation and night vision as routes for the exploration of or demonstration of vitamin-A deficiency, then we must recognize that the academic variations in dark adaptation which have been shown to exist in this country by various observers are far removed from the field of "A" deficiency disease and do not afford a pointer of any great clinical significance. To me it is almost inconceivable that any ordinary individual in Britain on fair average diet could suffer from manifest clinical evidence of "A" deficiency. A patient with such evidence would probably recover if given two meals a week equivalent to the main daily meal of a British soldier.

A second concerns skin rashes. Some years ago academic work in this country led us astray with regard to skin diseases in "A" deficiency. Any sort of skin rash in an undernourished child was supposed to be due to lack of Vitamin A. Those who worked in the midst of "A" defective populations only recognized one main skin rash as peculiar to the condition, namely pilosebaceous hyperkeratosis (variously termed phryoderma, pityriasis rubra pilaris, lichen acuminatus). This characteristic affection of the skin was used as an index in "A" deficiency surveys in Ceylon and Southern India, yet it is doubtful if the average ophthalmologist in this country would recognize the lesser degrees of the eruption if he saw it. It is clear that we must not divorce the clinical from the academic. The same holds good for riboflavin deficiency. I have yet to see a genuine ariboflavinosis corneae in this country, but since Sydenstricker's work, one would think from the observations of ophthalmologists that it was widespread; and accordingly riboflavin therapy has boomed on the strength of variations in the limbal vascular plexus, which are for the most part within normal limits for climate and occupation.

Dr. W. D. Wright said that in *Nature* R. A. Morton had made the definite statement that cone vision was improved with vitamin A. He himself expressed no view on this question, but if the fact was established, then it would tend to support the theory that cone vision was related to visual purple. He took it that Captain Yudkin's results were doubtful on this point—sometimes cone vision was affected and sometimes not.

Mr. D. V. Giri asked whether it was not possible that in these cases in which there was a deficiency of vitamin A there might be a lack of balance with some other vitamin in the body. Stress had been laid on vitamin C as a factor in the improvement of dark adaptation of people, but vitamin C had not been referred to by speakers on that occasion. As regards the difference in the dark adaptation of village school children and school children in Cambridge, which had been pointed out by Captain Yudkin, he wondered whether the difference between the two groups in mental alertness had anything to do with the differences noted. One would naturally suppose that the village children were getting quite sufficient vitamin A.

Mr. F. A. Juler, speaking with regard to the greater difficulty in dark adaptation with increasing years, suggested that this might be explained by fine changes in the outer layers of the retina. He had not seen any description of it in the textbooks, but he had frequently noticed a pigmentary change, simulating retinitis pigmentosa, in the periphery of elderly fundi, although to ordinary tests there was no contraction of the visual fields.

Dr. Z. A. Leitner said that Major Wright's constructive criticism based on his extensive experience in dealing with a population whose diet was one of the poorest in vitamin A in the world prompted him to mention the clinical evaluation of some results obtained recently at St. Mary's Hospital, W.2. Together with Dr. T. Moore (M.R.C. Lab. Cambridge) he had been investigating for the last sixteen months a large number of different conditions with regard to the vitamin-A content in the blood. They had been impressed by the widely conflicting reports published by different groups of workers in continental Europe and America who used the method of dark adaptation as an indicator of the state of vitamin-A nutrition. Their own method was the chemical estimation of vitamin A and carotene in the blood and through the kindness of Air Comm. C. P. Livingston the dark-adaptation threshold was also measured in those cases which showed definitely low vitamin-A values. The most extravagant claims for vitamin-A deficiency had been published in different diseases, mainly in skin conditions such as eczema, psoriasis, lupus vulgaris and erythematosis, syphilis and allergic dermatitis. The only diseases where they could find definite low vitamin-A values apart from unrubra pilaris (Devergie's disease). The interpretation of their findings was, however, not easy, e.g. only one of six Darier cases had had lowered dark-adaptation threshold. The dark adaptation was normal in two cases with pityriasis rubra pilaris and whilst a mother had normal vitamin-A and carotene level in the blood, those of her son were constantly low, and only after long-continued massive doses of vitamin A could the values be raised to, and above, normal level.

With regard to Dr. Pollak's interesting curves after yeast therapy, beside the influence of dietary intake and the rate of intestinal absorption of vitamin A, there were other factors in the determination of vitamin-A level, e.g. increased requirements for vitamin A by the different organs (e.g. in thyrotoxicosis), enhancement of the vitamin-A level by the synergistic action of vitamin E and lastly the difficulty of mobilization of vitamin A from the liver under certain circumstances. Excess of vitamin A was stored in the Kupffer cells, the normal storage seemed, however, to occur in the parenchyma cells of the liver. Vitamin A and carotene were absorbed after fission or hydrolysis in the small intestine by means of the pancreatic enzymes and the free vitamin A was transferred across the intestinal wall with the help of bile and arrived through both lymphatics and blood-stream to the organs, especially to the liver. The transport of

itamin A might occasionally suffer some kind of blockage either at the stage of transference from the liver to the blood, or from the blood-stream to the retina. In the first case both the blood vitamin-A level and dark adaptation might be affected, in the second only the latter.

Dr. H. S. Stannus said that it would be interesting if Captain Yudkin would add to his paper a note on the preparation of vitamin A used.

Mr. Godding, in reply, said that it was of great practical interest, and of obvious importance in the maintenance of health, to diagnose early changes. The most important of the known causes of failure of dark adaptation were, first, age; secondly, visual defects; thirdly, ocular and general disease conditions; then neurological and psychological causes, and the very important metabolic and nutritional causes group. He wished to add that although they had been discussing vitamin A he was sure that Captain Yudkin would agree with him that vitamin A was only one of the factors in this large and important group, and that very little was really known about it. He had recently been associated with one of the honorary staff of the St. John's Skin Hospital in carrying out a survey on a cross-section of the out-patient department, and they had not been able to find any significant difference in dark adaptation in a group of skin cases as compared with a group of controls. But in certain skin cases, among which was a case of pityriasis versicolor, it was possible to demonstrate quite clearly a correlation between dark adaptation and response to vitamin A.

Captain Yudkin, also in reply, said that he could underline what Mr. Godding had said about the importance of distinguishing early dietary deficiencies. He thought Major Wright would agree that there was something between deficiency disease and optimal health. If they were fortunate enough in this country to have little deficiency disease, they had nevertheless many people who were not getting an optimum diet and so far as any of these measures would help in detecting subnutrition, they were all of value. In Cambridge, for example, two groups of children were found in whom there was no evidence of vitamin A or C deficiency, but there was no doubt at all that the children in the poorer area were relatively worse nourished. The more tests they could devise to determine in what ways these children were inferior, the sooner they would be able to correct this inferiority. The fact that somebody had been given vitamin A and had improved did not necessarily mean that vitamin-A deficiency was implicated in the disease. This had happened in all vitamin work. As regards poor dark adaptation, there was evidence that other factors might be concerned. A number of people had been unable to show that vitamin C, which was also suggested, was concerned. But the results of treatment seemed to show that vitamin A was not the only vitamin implicated.

Amongst the Cambridge children a number of tests were carried out, including tests of intelligence and of educational attainment, and no correlation at all was found between the response to dark-adaptation tests and the results of these other tests.

Mr. Juler had suggested that retinal changes might be one of the causes of the deterioration in dark adaptation with age. All he would suggest was that the one factor of diminution of pupil size seemed to account quantitatively for the change.

The question of cone threshold and vitamin A was answered by saying that deficiency of the vitamin sometimes affected it and sometimes did not. **Dr. Leitner** had suggested that in some skin diseases there was a low vitamin A in the blood but no change in dark adaptation. That fitted in with observations recently made on experimental subjects and might be explained by the enormous stores of vitamin A in the body. The vitamin content in the retina might be kept up from this source for a considerable time even though the blood level fell rapidly.

In reply to **Dr. Stannus**, **Captain Yudkin** said that the preparation of vitamin given to the Birmingham workers and the Cambridge senior school was Multivite B.D.H. (5,000 I.U. vit.A, 1 mg. vit.B., 25 mg. vit.C, 500 I.U. vit.D) daily for one year. For the others, 100,000 I.U. vit.A had been given daily for twenty-one days.

The Herbert Iris Incarceration Method of Operation for Glaucoma

Dr. Mary Cripps gave a demonstration of the visual fields before and after operation. She had used the Herbert iris incarceration method in 306 cases, and the following were her conclusions as to the result.

I.—GLAUCOMA WITH TENSION RANGING FROM NORMAL TO 70 MM.HG (SCHIOTZ)

In those cases of chronic glaucoma whether or not an acute or subacute attack has been superimposed on the chronic state, and where the tension varying from 25 mm.Hg to 70 mm.Hg can be reduced (by appropriate methods) down to about normal and where the field of vision varies from a sickle-shaped scotoma and peripheral depression (early stages) down to the more advanced stages of a restricted field and sloping edged defects with depression of central vision—provided that not more than half of the fixation area within the 5 degrees circle has been invaded—then the vision improves with the Herbert operation.

II.—GLAUCOMA WITH TENSION ABOVE 70 MM.HG

Those cases where suddenly acute or ordinarily chronic where the tension which has risen above 70 mm.Hg, which can be reduced by intravenous glucose to normal limits but which rapidly rises again and where the vision is reduced.

(a) In those cases where more than half of the fixation area has been invaded and there are doubtful areas of vision, the operation gives only relief of pain and tension, and the vision is liable to deteriorate.

(b) In those cases where vision is reduced to perception of light in the upper temporal quadrant the Herbert operation gives increased vision in this quadrant with reduction in tension to normal limits.

However in these cases the operation must be modified; the edges of the incision are punched with a Lagrange punch before the fibrotic strands of the permanently dilated iris can be incarcerated.

Sclerosis of lens which may exist in these cases of prolonged tension is inclined to increase but as soon as the sclerosis has progressed sufficiently the lens is easily removed because the gap in the iris already exists and the fibrosed iris tissue of the filtering scar lies deep to the cataract incision. The wound heals normally without subsequent increase of tension.

Retinitis Circinata of Unknown Origin in a Child.—O. GAYER MORGAN, M.Ch.

Boy, aged 8. His mother said he was complaining of difficulty in reading. Vision was 6/18 in the right eye, 6/5 in the left. The fundus showed very marked retinitis circinata, with a small reddish or orange central spot which was just above the macula. The only relevant history was that he had had concussion a year previously, was bruised on the right side of his face, and the eye was closed. He was perfectly healthy except that he suffered from asthma. He had a very large head, which might denote a mild degree of hydrocephalus, but it was a family trait to have large heads. His condition, presumably, was one of oedema plus hæmorrhages, and it might be considered a case of early Coats's disease; the points against this were that there were no engorged or large vessels, or angiomatous-looking enlargements, no deep swelling, and no detachment. It might be a hæmorrhagic condition as a result of the fall, but it was a little difficult to see how it could cause such retinitis circinata. It might be one of those types of oedema of the retina usually unilateral, occurring in children or young people for no apparent reason, and in which no actual cause or pathology was known. He was anxious to know whether anyone had seen anything like this before.

The President said that he presumed it might be traumatic if, as a result of concussion, he had extensive choroidal hæmorrhage with damage to the macula, the retinitis being developed subsequently to that.

? Left Conjunctival Epithelioma. ? Atypical Mooren's Ulcer Superimposed on Old Mustard-Gas Damage.—ALAN HOLMES-SMITH, M.B.

Male, aged 60. Trolley-bus driver.

History.—1918: Damage to left eye by mustard gas. Three months' hospital treatment. Two to three months ago the left lids became swollen. This receded on treatment by hot bathing. In the three weeks before examination there was ptosis of the left lid.

Right vision 6/24. Left vision: counts fingers.

Right eye is normal on examination. The left shows an inactive pupil and no red reflex. Left tension is normal. There is a firm raised area of conjunctiva below and medial to the limbus extending into the lower fornix; the edge is raised. The lower nasal quadrant of the cornea is involved in the lesion and an opaque area separates it from normal cornea. No enlarged glands are palpable in the neck.

POSTSCRIPT (8.2.45) Pathological findings.—Mr. Holmes-Smith said that there was some difference of opinion as to the diagnosis, as to whether it was an atypical Mooren's ulcer or a new growth. It was finally decided to enucleate the eye, and that was done complete with as much conjunctiva as could be taken from the lower fornix. On section the tumour was thought to be an epithelioma with considerable inflammatory reaction, with the sclera undergoing invasion at the limbus. The radiotherapeutic department, at St. Thomas's considered it wise that he should have a course of treatment there; details are not known as no report has yet been sent.

Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[December 5, 1944]

Experimental Observations of the Use of Absorbable and Non-absorbable Plastics in Bone Surgery

By Captain GEORGE BLUM, R.A.M.C., B.R.S. Pool, War Office
(Department of Physiology, Middlesex Hospital Medical School, London)

Two main classes of materials were employed in the course of this experimental investigation: (1) non-protein plastics of varying composition; (2) protein plastics.

(1) *Non-protein plastics*.—The chief plastics of this class that have been studied are: Methyl methacrylate (Perspex); cellulose acetate; nylon; urea formaldehyde; phenol formaldehyde. Experimentally, methyl methacrylate proved to have the most satisfactory characteristics and, in the later work, it alone was studied in detail from the point of view of surgical applicability.

(2) *Protein plastics*.—The chief protein plastics studied were made up from: Casein; fibrin; casein with plasma; red blood cells; whole blood. These plastics resemble one another in their physical and physiological properties, differing only in their quantitative characters. The protein plastic chiefly studied was casein plastic. One fundamental and surgically important difference was established between the non-protein and the protein plastics. The non-protein plastics are not absorbable in animal tissues; the protein plastics, on the contrary, are absorbable, the rate of absorption depending on various factors. The protein plastics used were formalized by immersion in 4% formalin for periods of one to fourteen days or fully formalized.

They can be machined to provide screws, plates, blocks (that might be used for grafts), tiffin nails and other objects.

The strength of these protein plastics is not in the same class as the metals but is of the same order as that of bone. Strength increases with the degree of formalization but decreases if the material is stored under unsatisfactory conditions.

The protein plastics are in time completely absorbed in the tissues giving rise to little, if any, permanent fibrous tissue reaction. The speed of absorption depends on: (1) the degree of formalization, fully formalized material being the slowest; (2) the bulk of the implant; (3) the tissue in which it is placed. When a protein plastic is implanted in tissue it first becomes rubbery and can be cut with a knife with difficulty. It then becomes progressively softer and cuts easily. The surface becomes granular and cheesy in appearance. It then becomes quite soft and breaks up into granular particles in a

semi-liquid matrix. Finally, the entire plastic becomes mucoidal, then more fluid and finally completely disappears as a result of absorption. A capsule of fibrous tissue is formed in the course of absorption and at an intermediate stage may be fairly thick. Usually, however, when the plastic has disappeared the fibrous reaction is found to be greatly diminished. Implanted in bone, protein plastic undergoes absorption similarly. It is replaced, as absorption proceeds, by newly formed bone.

Protein plastic screws, of a size suitable for use on the tibia of a cat or a rabbit, were completed absorbed in four to six months. The speed of absorption was in inverse ratio to the degree of formalization. The much bulkier screws that would have to be employed in clinical trials might take a much longer time to disappear. No rarefaction takes place in the bone round the screws. The replacement of the screws by fresh bone takes place as fast as the screw disappears.

The mechanism of softening and absorption of the screws has not yet been studied in detail. Softening and liquefaction are partly due to the action of proteolytic enzymes which break down the casein or fibrin of the plastic into the usual soluble simpler derivatives like peptones or polypeptides. There may be, at an intermediate stage, a heavy cellular infiltration of the margins of the softened plastic.

The most sensitive index of tissue response to foreign bodies is their effect on explants of living embryonic tissue in tissue culture. Miss Honor Fell, of the Strangeways Laboratory, has carried out such tests which showed the harmlessness of these protein plastic materials. It should be borne in mind, however, that results obtained in lower animals do not necessarily or wholly apply to man. No evidence of allergy has been obtained in animal experiments. Protein plastics have been inserted on several occasions in the same animal without harm.

These plastics are satisfactorily sterilized by autoclaving for twenty minutes at 120° C.

It is concluded that: the protein plastics employed are not harmful to the tissues; they are completely absorbed in soft tissues and in bone; when inserted in bone they are completely replaced by new bone.

Non-absorbable plastics.—Plastics derived from non-protein sources are not changed or absorbed in the soft tissues or in bone. Individual compounds vary in the degree of tissue response which they produce. Experiments by Miss Fell show that some of them kill explants of embryonic tissue in tissue culture. Methyl methacrylate, however, produces no deleterious effects. In general, the gross responses of animal tissue to the presence of these non-absorbable plastics agree with the findings of Miss Fell. Frequently, however, even the plastics which are most lethal to tissue cultures produce little gross tissue reaction. Because of its biological and physical properties, methyl methacrylate was chosen for more prolonged and detailed experimental study.

Methyl methacrylate plastic is perhaps stronger than casein plastic, but it is not in any way comparable in strength with steel. A long series of experiments was carried out using methyl methacrylate plates, tubes and screws in the treatment of fractures in experimental animals. The results suggested that this plastic used in this manner has no outstanding advantages over the metals and has the disadvantage of being a much weaker material.

Methyl methacrylate is widely used clinically at present for different purposes, e.g. in the manufacture of dental base plates, artificial teeth and dental fillings; for Gunning splints used in the treatment of fractures of the mandible in edentulous patients; and for the filling of gaps in the cranium. The technique employed at present takes two to two and a half hours in the hands of an experienced dental technician and involves a second surgical operation.

Methods have been adopted which enable methyl methacrylate to be used for these and other purposes in a much shorter time (about fifteen minutes). If such procedures were employed, for example, in the filling of skull gaps they would enable the operative treatment to be completed in one sitting. The principles employed are as follows:

First method.—Unplasticized methyl methacrylate sheet is thermoplastic, i.e. methyl methacrylate sheet to which no plasticizer has been added, will, on heating to 130° C., become soft, pliable and easily mouldable to any desired shape. On rapid cooling, this shape is retained. Sterilization in the autoclave or by boiling does not cause loss of shape. In the case of plasticized methyl methacrylate on the other hand, this heat treatment causes deformation. We have been able to obtain moulded methyl methacrylate prostheses by a method based on the principle outlined above; the whole proce-

dure taking about fifteen minutes. This method may be of interest to those who use methyl methacrylate in dental, facio-maxillary and cranial surgery.

Second method.—This method makes use of the fact that methyl methacrylate dough containing a special catalyst will undergo hardening and polymerization when exposed to ultraviolet rays for fifteen to twenty minutes at a temperature not exceeding that of the body.

Experiments on animals have shown that methyl methacrylate dough inserted into a skull gap and irradiated as described produced no dural reaction or changes in the underlying brain tissue. Some ossification also took place across the floor of the gap between the plastic and the dura. Methyl methacrylate dough treated as described has also been tried out for experimental spinal fixation. No harmful effects were observed.

(A full report will be published in the *Lancet*.)

[The cost of the research was defrayed by a grant from the Medical Research Council.]

Cancellous Chip Grafts for the Restoration of Bone Defects

By A. RAINSFORD MOWLEM, F.R.C.S.

Success in transplanting any avascular tissue is dependent upon many factors, of which at least two are essential. The first is that the new bed shall be capable of providing an adequate blood supply and the second is that the transplant shall be of such a nature that, if it be kept in accurate contact with the recipient area, vascular continuity can be established early enough to ensure cellular survival. Failure to produce and maintain these conditions will result in disaster.

More than a hundred years ago Charles Bell wrote: "Scrape a bone and its vessels bleed; cut a bone and its granulations sprout up; break a bone and it will heal; cut a piece away and more bone will readily be produced; burn it and it dies." On the whole this statement is descriptive of modern experience, so that we agree bone is an active and vascular tissue, and it is difficult to see why the transplantation of bone can be independent of those factors which determine success in the grafting of other tissues. Some of our modern methods of grafting, and the tissue used therein, owe more to carpentry than to the consideration of biological requirements. This state of affairs has arisen because the material chosen as the graft has been selected for its stability and not its viability. Rigidity is conferred, if living tissues are to be used, only by a structure with a high inorganic content—viability demands a degree of cellularity which is not found in dense bone.

If these two characteristics are not co-existent, the problem of which to choose to the exclusion of the other becomes of real importance. Hitherto we have sought stability and have obtained it, but I think that we have done so at the expense of some uncertainty of results, of considerable slowness of regeneration and of a fairly high potential of infection. We have become accustomed to the time factor, and have worked out theories which explain it, but which in my opinion do not cover the potentialities of the process of grafting.

I suggest that if our desire is to transplant bone which will survive from the time of its insertion, which will not be a bridge across or in which "creeping substitution" may occur, but which will be an active living tissue rapidly acquiring continuity with the bone ends, then we should lay much more stress on viability than on stability.

A fairly considerable experience with cancellous bone for reconstructive work has shown that this type of bone possesses characteristics which differ from those ascribed to cortical transplants.

Firstly, it very rapidly undergoes the changes necessary to suit it to its new location—for example, a new cortex is clearly marked on X-ray investigation in eight or twelve weeks. Secondly, it can withstand infection to an unusual degree. This capacity increases with every day which elapses between transplantation and the occurrence of the infec-

tion. Thirdly, neither of these characteristics nor the permanence of its survival depends upon its acquiring continuity with other bone, but they are contingent upon an adequate vascular supply.

These findings, together with histological considerations, led to the belief that this type of bone survives transplantation and retains its cellular activity. This is almost certainly due to the fact that it is an open network of bony tissue containing many bone cells, most of which are so near to the surface that they can easily be reached by their new blood supply. Its structure, therefore, contrasts very sharply with that of cortical bone, which is a mass of densely calcified tissue containing tortuous Haversian systems with a few bone cells at their inaccessible distal ends.

Over three years ago it was felt that in order to take full advantage of the characteristics of cancellous bones, it would be justifiable to increase the surface area by fragmentation so that an even greater number of cells could acquire a new blood supply and thus survive their transplantation.

Chips have been used in over 80 cases for the restoration of losses of contour and of continuity. All the grafts have been derived from the iliac crest, and they have all consisted only of cancellous tissue, which has been cut into fragments about 1 cm. by 0.5 cm. by 0.2 cm.

For restoring contour of the facial or cranial bones, the chips are simply built up into the desired shape and kept in position by light bandage pressure maintained for five to seven days. Within that period adhesion to underlying exposed bone occurs, and clinical rigidity is obtained. The defect is therefore easily and permanently restored and by the employment of an entirely appropriate tissue (fig. 1).



Pre-operative.

Post-operative.

FIG. 1.—Restoration of frontal and nasal bone loss in the presence of a fistula in the left frontal sinus. The interval between the pre- and post-operative photographs is two months.

In 35 consecutive cases of mandibular losses with an average defect of two inches, clinical rigidity and the discontinuance of all splintage have been obtained in twenty-six days. Though it may be argued that the mandible is not a weight-bearing bone, it should be pointed out that the average pressure on the biting surface of the teeth may be anything from 100 to 200 lb. per square inch.

For restoring continuity, we must rely on alternative means of obtaining stability. In this series, skeletal pin fixation or plaster casts have so far been sufficient, but in some situations it seems probable that internal splintage will be desirable. This may well be provided by either cortical bone or by plating. The former is possibly preferable because of the advantage of using a material which can be subsequently incorporated in the repair, though there are two potential disadvantages. Firstly, the bulk of the graft will tend to deprive some of the underlying chips of their blood supply, and secondly, the widespread separation of periosteum from the shaft, so often associated with the process of insertion, may diminish the vascular input to the bone ends.

Once stability is obtained, all eburnated bone is widely removed, and as much scar as possible excised from between the bone ends. The requisite bulk of shaft is then built up by cancellous chips, which will need no fixation other than suture of the soft tissues over them. Union between the chips themselves and the exposed bone ends occurs rapidly, and it is of interest to note that clinical rigidity precedes complete radiographic fusion.

Fig. 2 illustrates the radiographic appearances at ten weeks, when the first below-knee walking plaster, which had been applied five weeks earlier, was changed. At fifteen weeks this plaster was replaced by a light guard plaster, allowing a full range of movement at the knee and ankle, and controlling only any possible tendency to angulation. This was removed at twenty weeks, and thereafter no further treatment was given.

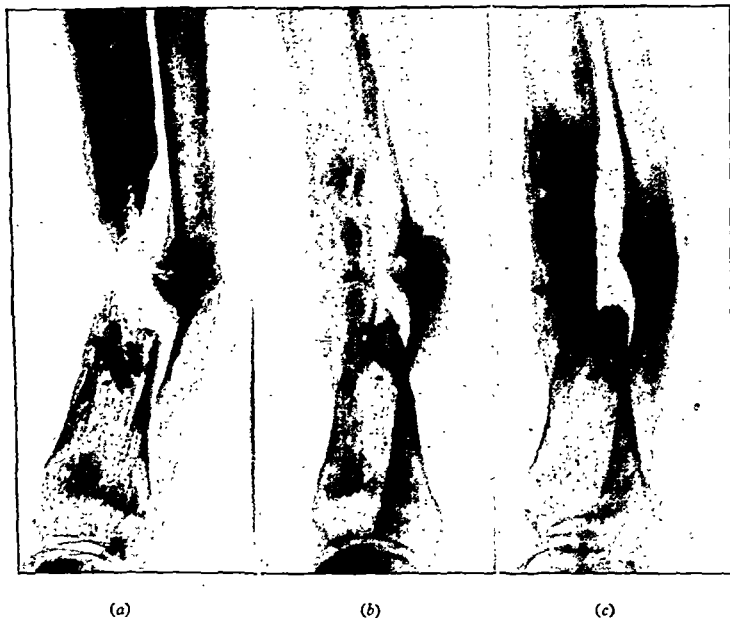


FIG. 2.—A reconstruction of a tibial shaft by bone chips. Pre-operative condition shown (a). Condition at ten weeks shown (b). It will be seen that fusion between the chips is not yet complete though the bone is clinically rigid. Condition at fifteen weeks shown (c). The condition of the cortex in the depths of the wound is much more clearly defined than in the subcutaneous region. This is due to a relative inadequacy of blood supply in the latter region.

My personal experience of grafts to limbs has been limited to those unfortunate cases of compound fractures of the tibia which are referred for treatment with skin and bone loss of many months' duration and in which the vascularity of the whole limb is grossly insufficient. In spite of this initial difficulty, one case with a one inch tibial defect was walking without splintage in ten weeks, while others with defects of between three inches and four inches were weight-bearing in a below-knee plaster in five weeks, and discontinued all splintage in twenty weeks. Some of my orthopaedic colleagues can show even more spectacular results in the commoner type of linear non-union, which in some instances have been capable of normal unsupported weight-bearing in six weeks.

There is another aspect of the behaviour of these grafts which is worth noting, though this characteristic is shared to some extent by all cancellous grafts, whether they be fragmented or not. Resistance to infection is very much greater than that possessed by cortical bone. In at least eleven instances grafts have been inserted in areas known to be infected. Six mandibular defects with sinuses into the mouth were treated. In another there was an area of residual osteomyelitis at one end of an extensive defect in the jaw; at the same time there was a fistula into the mouth. The area of infected bone was excised, the fistula sutured and the defect grafted by chips. It is true that a penicillin tube was inserted, and a thousand units a day were given for a week. At all events, the graft was satisfactory. At least two infected defects in cranial bones have

been widely excised and grafted, and in these also the result has been good. Two cases of tibial defect infected with *Staphylococcus aureus* and with *Ps. pyocyanea* respectively have also been treated, and though it may be argued that the good results obtained in all the infected cases have been due to penicillin, this cannot be true of the latter case, because the organism concerned is resistant.

The implications of this characteristic appear to me to be very important. No one would suggest that it is desirable to insert a bone graft in the presence of sepsis, though we have deliberately done this in an endeavour to evaluate the tolerance of the tissue. Much more work remains to be done, but it does seem probable that the presence of low-grade localized infection need not be a barrier to bone grafting. If such grafting can be carried out before long-continued disuse has resulted in irremediable atrophy of the locomotor and vascular systems, then not only is much time saved, but the resultant limb will approximate much more closely to normal. The application of this principle to battle casualties may go far in reducing the incidence of chronic sinuses and ununited bones.

If, therefore, we are to adopt a biological standard as the basis for our technique in bone grafting, it is clear that we shall have to choose a less rigid and more cellular type of bone than that usually employed. We shall do well to increase the surface area by fragmenting the graft, and therefore we shall need to rely on something other than the graft itself for the provision of immediate stability of the bone ends.

Modern methods should not find this an insuperable difficulty. We must learn to create and conserve blood supply under all circumstances, and this may mean giving up wide subperiosteal exposures and beautifully carpentered joints. In return for these losses, we may find a considerably simplified technique which can be applied earlier, with more certainty and with much more rapid results than has hitherto been associated with bone grafting.

Section of Obstetrics and Gynæcology

President—S. GORDON LUKER, F.R.C.O.G.

[November 17, 1944]

Principles of Treatment of Carcinoma Cervix Uteri by Radiotherapy

By BERNARD SANDLER, M.D., D.M.R.
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For the purpose of this lecture radiotherapy will be taken to include X and γ radiations only. This type of treatment has hitherto rested very largely on an empirical basis.

The radiotherapist tries to deliver a dose of radiation which shall be lethal to the cancer cells both in the primary tumour and in the potential sites of invasion. The problem can now be separated into two parts.

(1) How does the radiation act, and what is a lethal dose?

(2) Where and how shall such dose be delivered? i.e. what is the site, extent and position in relation to the pelvis both of the primary tumour and the possible secondary paths of invasion, for the whole of this volume must be included in the tissues to be treated.

These two questions summarize crudely the nature of the biological and physical problems to be solved before success with treatment can be achieved.

A. Biological problems.—These involve the choice of wavelength, dosage rate, spacing of treatments, total dosage, &c. In turn they depend on an understanding of the behaviour of both normal and malignant cells exposed to radiation.

Radiation can induce either a temporary or a permanent effect, or both, on cells normal and malignant. One temporary effect is the suppression of cell division, the duration of which depends on the dose given.

There is on the other hand experimental evidence (Sax, 1941; Muller, 1941) that with a relatively small dose (5 r to 600 r) the death of the cell is brought about by the damage sustained during the resting stage in the nucleus, particularly to the chromosomes. This damage is due to direct ionization, and it is observed in the next mitosis when there are broken chromosomes and chromosome fragments present in the dividing cell (figs. 1 and 2). The daughter cells being deficient in their nuclear content will die. The damage to the nucleus of the cell, resulting in its death, is a *direct* radiation effect. If several adjacent cells die simultaneously, after a dose of, say, 1,500-2,000 r, there will be a change in the histological organization of the tumour tissue; any local failure in blood supply will also cause a breakdown of a still larger cell population.

With the break-up of the tumour parenchyma by cell degeneration, the response of the tumour-bed, i.e. an *indirect* effect of the radiation, comes into play. Infiltration and subsequent differentiation of cells of the reticulo-endothelial system (plasmacytes, histiocytes, lymphocytes and cells of the granulocytic series) form part of the repair process.

The problem is how to control both the intracellular radiation effects and the inter-cellular response. If cells are killed rapidly and in too great a number, or if the tumour-bed is damaged, the repair process will be unable to function properly and fibrosis may occur prematurely. Cytological analysis of the radiation effects is of the utmost importance especially at the stage when the intra- and inter-cellular processes are in progress if we are to assess the degree of the biological response of the tumour and control the treatment.

been widely excised and grafted, and in these also the result has been good. Two cases of tibial defect infected with *Staphylococcus aureus* and with *Ps. pyocyanea* respectively have also been treated, and though it may be argued that the good results obtained in all the infected cases have been due to penicillin, this cannot be true of the latter case, because the organism concerned is resistant.

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FIG. 1.—Dividing cell of the newt in metaphase, fixed eight hours after an exposure to 15 r. Some of the chromosomes show breaks induced by the radiation. $\times 2,300$.



FIG. 2.—Dividing cells of the newt in anaphase, fixed eight hours after an exposure to 15 r. The chromosomes move towards the opposite poles except a fragment, which was broken off a chromosome as a result of the radiation. $\times 2,300$.

(Figs. 1 to 4 prepared by P. C. Koller, Ph.D., D.Sc.)

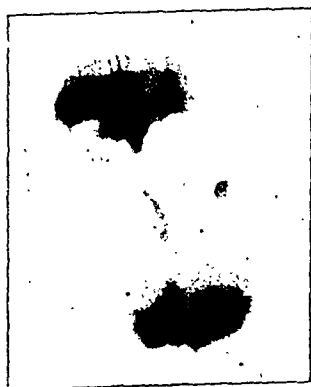


FIG. 3.—A dividing cell from squamous-celled carcinoma of the cervix, fixed twenty-four hours after an exposure to 100 r. Two small chromosome-fragments are left behind the other chromosomes which form the nuclei of the two daughter cells. $\times 3,200$.



FIG. 4.—A dividing cell from squamous-celled carcinoma of the cervix, fixed seven days after a twenty-two hours' exposure to 50 mg. of radium. The chromosomes are broken into very many fragments. $\times 3,200$.

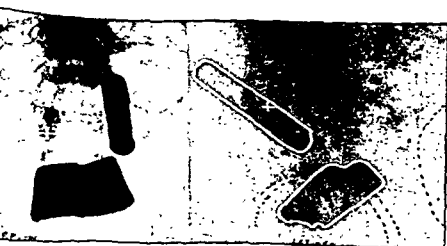


FIG. 5a.—Lateral deviation of uterus and overlap of boxes. Dosage unequal to the two sides of the pelvis.

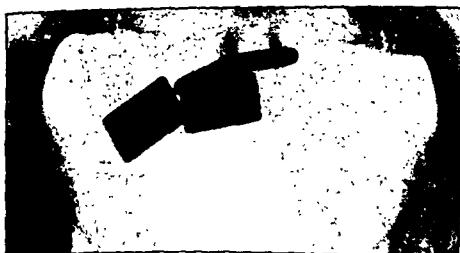


FIG. 5b.—Lateral deviation from mid-line, with acute anteversion and lateral inclination of uterus. Unequal dosage to pelvic wall. Antero-posterior view.

We may here instance a series of cases in which we delivered to a squamous carcinoma of the cervix exactly 100 r by X-ray and twenty-four hours later took pieces of tissues for biopsy. Although the tumours were histologically similar, great variation was observed in the response: in one case only 5% and in another 45% of the dividing cells showed radiation-induced chromosome abnormalities. Since the ultimate death of the tumour depends upon the production of these abnormalities and the frequency of cells affected, clearly a different type of treatment will be required for two such tumours showing so wide a variation in cytological response. It would seem illogical to give the same dose to each of them—yet that is what happens so frequently with the standard techniques in use to-day.

It may be possible to use radiation more economically by taking into account the biological response of individual tumours which may permit us to use lower total dosages than we have hitherto applied. It is clear that standard fractionation (e.g. Stockholm) is not adapted to individual requirements in this respect. Such procedures would overcome the serious obstacle of the inability of the normal pelvic organs to withstand the very high dosages considered necessary in present techniques, failure to achieve which has been responsible for a high proportion of recurrences.

To the question "What is a lethal dose?" there can be therefore no fixed and simple answer applicable to all tumours of a given organ or tissue as assumed by some workers. We have some evidence that satisfactory tumour regression can be obtained by taking into account the biological response and adapting the treatment to the individual requirements of the tumour. Glücksmann and Spear (1939) and Glücksmann (1941) have already shown that tumours apparently similar histologically may respond differently to the same type of radiotherapeutic procedure.

Control of the intracellular and of the intercellular effects of radiation during treatment is desirable, and the cytological findings suggest that much of the radiation given at present may either be wasted because it is delivered without regard to the biological behaviour of the tumour cells, or may be actually harmful as it may damage the repair process. It is possible that cytological research can provide a more scientific basis for a treatment plan for carcinoma of the cervix to replace the empiricism upon which dosage has been administered so far. Tradition (and perhaps inertia!) has maintained the practice still widely observed, first established by Försell in 1910 and elaborated by Heyman, of the intervals of seven and then fourteen days between successive radium treatments. Except that shorter intervals produced severe reactions with these weights of radium, apparently no other scientific reason has been given for just these particular spacings. Whilst there has been abundant experiment with the time factor ranging from an overall time of three hours in America to as much as six months by Mallet (1936) in Paris, and all have been successful on occasion, these methods have not been based on scientific observation of the reaction of the cells of each tumour to radiation. Indeed, administrative reasons such as the availability of the theatre, or lack of radium or apparatus may have been a more important factor in the choice of a particular spacing!

Cytological research is especially needed for carcinoma of the cervix (i) to discover the effectiveness in timing and spacing of the single and cumulative radium insertions, (ii) to correlate the physical dose (ascertained from isodose curves, &c.) with the biological effect based on the cell response. Such data will decide in each individual case such questions as: (a) Is a twenty-four-hour radium insertion necessary? (b) Is a seven- or fourteen-day interval necessary—if not, what is the best? and (c) How shall the weight of radium be varied? Information so gained may enable us to determine what is the best combination of X- and γ -rays from a biological point of view. It may well be that we shall have to use radium either more or less frequently and at variable intervals, for there is no doubt that by the present generalized methods we are applying standard doses to tumours differing greatly in their biological behaviour and these doses, whilst producing a direct caustic action in one place, are completely ineffective in another.

Fig. 3 shows a cell in which two small fragments are broken off the chromosomes induced by 100 r. Fig. 4 shows another cell with a very great number of fragments, produced by a twenty-two-hour exposure to 50 mg. radium. In the first case, the death of the tumour cells occurs in the next generation due to a failure in the nuclear control of normal metabolic activity caused by chromosome deficiency. In the second case there is a physical disintegration of the parent cell due to the very high dose of radiation received; an unnecessary, uneconomical and biologically even harmful process because the same dose can induce similar damage to normal cells.

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FIG. 1.—Dividing cell of the newt in metaphase, fixed eight hours after an exposure to 15 r. Some of the chromosomes show breaks induced by the radiation. $\times 2,300$.



FIG. 2.—Dividing cells of the newt in anaphase, fixed eight hours after an exposure to 15 r. The chromosomes move towards the opposite poles except a fragment, which was broken off a chromosome as a result of the radiation. $\times 2,300$.

(Figs. 1 to 4 prepared by P. C. Koller, Ph.D., D.Sc.)



FIG. 3.—A dividing cell from squamous-celled carcinoma of the cervix, fixed twenty-four hours after an exposure to 100 r. Two small chromosome-fragments are left behind the other chromosomes which form the nuclei of the two daughter cells. $\times 3,200$.

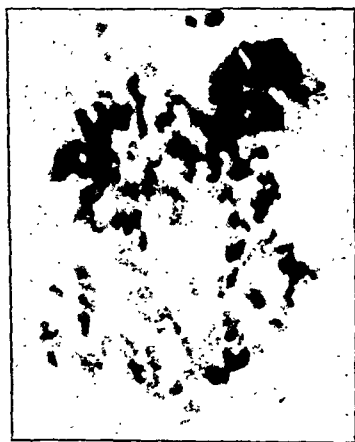


FIG. 4.—A dividing cell from squamous-celled carcinoma of the cervix, fixed seven days after a twenty-two hours' exposure to 50 mg. of radium. The chromosomes are broken into very many fragments. $\times 3,200$.

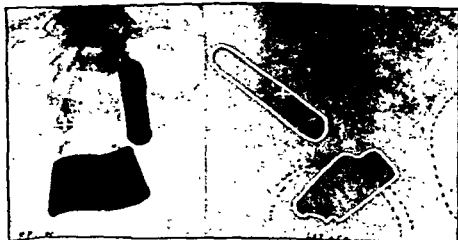


FIG. 5a.—Lateral deviation of uterus and overlap of boxes. Dosage unequal to the two sides of the pelvis.

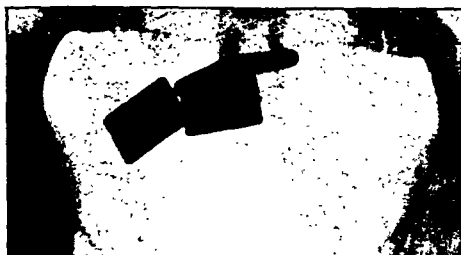


FIG. 5b.—Lateral deviation from mid-line, with acute anteversion and lateral inclination of uterus. Unequal dosage to pelvic wall. Antero-posterior view.

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demonstrate the summation of dosage. By placing them in the correct positions we may see the effect of high and low spots of intensity from radium sources which are apparently in similar positions. Clearly then the distribution of dosage for each source of radiation must be determined if an effective treatment is to be planned. By the invention of the dose-finder, Mayneord (1939, 1941) has been able to produce the most complete models and charts hitherto published of volume distribution for a given technique. In practice, some considerable deviations occur from the theoretical physical dispositions which form the basis of these calculations. These variations occur in both the uterus and the vagina.

In the uterus, variations in length, the presence of fibroids, distortion by the carcinoma itself, lateral deviation, acute anteversion or retroversion will affect the dose delivered. In the vagina, the variations depend, *inter alia*, on the size, shape and distensibility of the vaginal vault and are not related in this respect to the stage of disease (Sandler, 1942a). These physical dimensions, therefore, have a primary determining influence on the positions of the applicators, and consequently on the lethal isodose surface produced (see *Brit. J. Radiol.*, November 1943, x6, 331, Table I, and Sandler, 1941). This influence may be much greater in some cases than that of the type of technique used in the particular size of vagina under consideration.

Alterations in the relative positions of the organs in the pelvis during and after treatment are frequent. Some of the more important of these factors which cause an alteration in the relative position of the organs may be:

(a) The presence or absence of packing, the degree of distension of the bladder and rectum and the posture of the patient.

(b) Regression of a large tumour or stenosis of a large cavity in the interval between X- and γ -ray therapy will distort the organs and render them unreliable for measurements of the position of the radium.

(c) Mechanical faults occur due to slipping of applicators. For instance the radiograph may show that the uterine tube does sometimes slip out of the os. More often a bulky cervix consisting mostly of tumour may disappear completely later. In either case the highest point of the vagina as ascertained subsequent to the radium treatment will be considerably higher than the position actually occupied by the lower end of the uterine tube during treatment. Unless this position is accurately determined when the radium is in situ it will not be possible to relate the X-ray distribution to it exactly at a later date. The radium then, rather than the organs which contain it, determines the positioning of the supplementary X-ray therapy and this knowledge must be available when the X-ray therapy is given.

By a special apparatus (Sandler, 1943) the position of the radium in situ in the bony pelvis may be recorded. In a series of 30 cases the cervix was found to be pushed in a cephalic direction by the packing to an average of 4 cm. above the level of the symphysis—the usual level given in textbooks.

This raises fresh problems for the X-ray therapist who has to correlate his radiation with that delivered by the radium. Figs. 5a and 5b show the bad effect of these individual factors on the same technique as used in two different hospitals. These bad effects may be summarized as:

(a) Vault stenosis forces the applicators down the vagina.

(b) The long axis of an object placed in the vagina tends to rotate so that it occupies the longitudinal axis of the vagina. This is often accompanied by slipping and overlapping of the applicators.

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It has been shown previously that each size of vagina must have its own variation of technique (Sandler, 1941) if full use is to be made of the available tolerances which differ with each size of vagina. The actual dispositions of the radium shown in these patients are, as might be expected, different from those anticipated in a theoretical technique. Thus if the doses received at selected points in the pelvis are based as a routine on what may be expected from these theoretical distributions, gross inaccuracies may occur. An error of 1,000 roentgens as between the right and left sides is not uncommon and a variation of up to 2,000 roentgens in dose delivered by the same technique may occur in different sizes of the vagina (Sandler, 1942a).

In order to illustrate the effects of slight variations in the disposition some hypothetical cases have been studied with the dose-finder. The simplest is a single vaginal box of 50 mg. radium content, filter 1.2 pt. In the absence of an agreed figure 5,000 r is taken arbitrarily, for illustrative purposes, as the minimum lethal dose, although this is probably much too small (see *Brit. J. Radiol.*, figs. 2a and 2b. 1943, x6, 332).

Provided the uterus is not retroverted, it is better (Sandler, 1938a) to reduce the radium at the cervix and increase it at the fundus, so long as a definite parametrial

ideas on dose fractionation and total dose. This can only be obtained from cytological research.

B. Physical problems.—It is now necessary to define the site, extent and position in relation to the pelvis of both the primary tumour and the possible paths of invasion. This presents a difficult problem in localization since only a portion of the tumour is usually accessible to vaginal measurements. Definition of the extent of the primary and selection of the total volume of possible secondary invasion are problems which overlap and are not often capable of a precise answer.

As will be shown later the practice of assuming that the radium will deal adequately with the primary and X-rays with the secondary tumour is by no means true. Whilst these two forms of radiation are complementary in that one should make up for the deficiencies of the other, it is rare to find that their respective spheres of effective action coincide with the anatomical limits of primary and secondary tumour. And indeed, there is no reason why they should.

The anatomical paths of invasion have been discussed in previous papers by many writers as well as myself (1938a, 1941). Sampson (1907), Taussig (1934), Martzloff (1923) among others have shown that even in the early stages spread to the lymph nodes of the lateral pelvic wall may have taken place whilst the growth is apparently still confined to the cervix. The frequency of such invasion in Stages 1 and 2 may be as high as 40% (Taussig).

One must, therefore, contemplate treating the whole of the true pelvis and even this may be too small a volume to include all the main sites of invasion since many patients have involvement of lymph nodes extending above the brim.

Although it is often asserted that the level of the iliac nodes is at the bifurcation of the iliac vessels—in turn said to be at the level of the pelvic brim—it is not uncommon to find both the bifurcation and the invaded nodes above the level of the brim (see Stone and Robinson, 1941, and Batson, 1940). [A slide was shown of an X-ray film showing spent gold seeds inserted for me at operation by Mr. Blaikley at the sites of the iliac lymph nodes. Distortion was avoided by centring over the sacro-iliac joints, and the seeds were shown to be well above the pelvic brim. Lack of space prevents the reproduction of this and other films here.]

Clearly then the volume to be treated must be not less than the true pelvis and should in many cases include more than that volume.

Building up dosage.—There is no doubt that the manner in which dosage is built up from multiple sources of radiation is not at all clear to some gynaecologists. It is perhaps inevitable that since they are concerned only with the placing of radium in the vagina they should tend to regard such applicators as satisfactorily placed when they are in close relation to the cervix and fornices. They may not realize that the volume of tissue receiving adequate dosage from that particular distribution of radium may not in fact enclose even the primary tumour visible in the vagina. The very name of applicator is misleading in this sense since it suggests a local action by contact, rather than the more distant effect of the radiation emitted by it, which is the real basis of radium treatment. The term "Radium Sources" is therefore preferable as indicating the mode of action.

No doubt historical reasons have preserved this fallacy. The very discovery of the biological action of radium rested upon its local caustic action on the skin. Only later in 1912 did Forsell elaborate his principles of heavy screening, low intensity and fractionation at seven- and fourteen-day intervals. Even then many who carried out his technique did not fully appreciate that they were dealing with a radiation—i.e. an effect on tissues produced at a distance from the source, and as such delivering to a given point an aggregate dose of radiation from the several individual sources not easily ascertainable. The "unit" milligram-hours served still further to stress unduly the radium itself rather than the radiation it produced. To state that the illumination of a room is a 40 watt lamp gives no idea of the adequacy of the wall illumination unless one knows whether it is a bathroom or a ballroom! To push the analogy further it is also clear that one might get adequate illumination even to a ballroom using lamps as low as 40 w. but it would require careful arrangement. That is the essence of the problem of vaginal radium distributions.

Isodose surfaces.—The problem of spatial distribution of dosage is fundamentally the same for both X- and γ -rays, except that radium as used here cannot be discussed as a point source. This whole concept of 3-dimensional distribution is due to Mayneord who first analysed the volume distribution of beams of radiation and devised methods (1941), of ascertaining these distributions and of expressing the results as isodose charts or as models. Based on his conceptions, Ungar (1943, *Brit. J. Radiol.*, 16, 274) has devised a simple way of making tinted isodose charts from waste films which clearly

demonstrate the summation of dosage. By placing them in the correct positions we may see the effect of high and low spots of intensity from radium sources which are apparently in similar positions. Clearly then the distribution of dosage for each source of radiation must be determined if an effective treatment is to be planned. By the invention of the dose-finder, Mayneord (1939, 1941) has been able to produce the most complete models and charts hitherto published of volume distribution for a given technique. In practice, some considerable deviations occur from the theoretical physical dispositions which form the basis of these calculations. These variations occur in both the uterus and the vagina.

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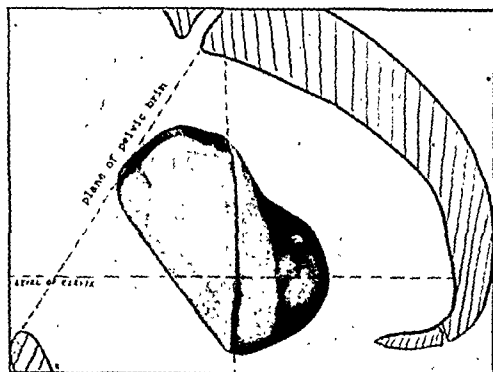


FIG. 6a.—Sagittal view of 5,000 r isodose surface of radium from fig. 5a.

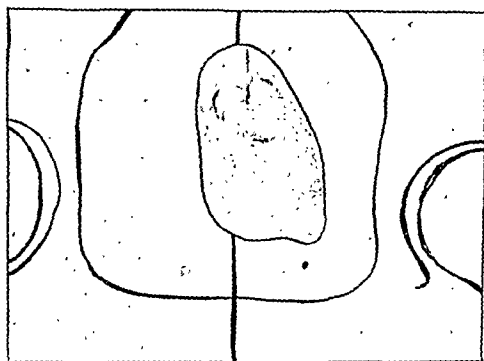


FIG. 6b.—Coronal view of 5,000 r isodose surface.

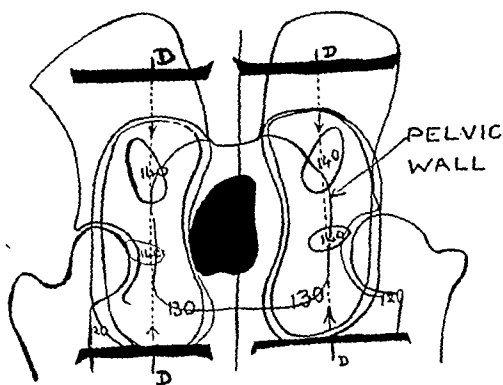


FIG. 9.—X-ray fields placed symmetrically to patient's mid-line. Black area represents lethal isodose surface of radium, and gap of underdosage is seen on patient's left.

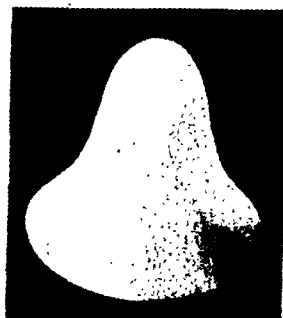


FIG. 7.—Isodose surface (6,000 r) of the Marie Curie technique. [By courtesy of Professor Mayneord.]



FIG. 8.—Distribution in r per hour in coronal plane by method of Sandler and Ungar.

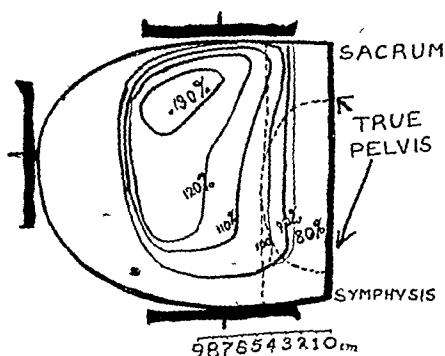


FIG. 10.—Dose distribution to pelvis at 400 kV. by Quimby method. Most of the radiation is outside the true pelvis.

(Figs. 5a, 5b, 6a, 6b, 9 and 10 are reproduced by kind permission of the Editor, *British Journal of Radiology*.)

tolerance has not to be exceeded (Sandler, 1938b and 1942b). In an actual case, before measurement on the dose-finder can be done, it is necessary to reconstruct the positions of the radium in space. The details of this have already been published (Sandler, 1943).

Fig. 6b shows the three-dimensional asymmetry in the coronal plane, and fig. 6a in the sagittal planes of the isodose surface. The distortion of the distribution in this case is striking when compared with fig. 7.

Dr. Ungar and myself (1944) have worked out a geometric method of obtaining dose distributions but it still requires some considerable time to carry out. It is hoped that this will be still further reduced by technical improvements. Fig. 8 shows what can be achieved in about an hour's work. This type of result may indicate what should be avoided and what corrected at the next radium insertion. Both the gynaecologist and the X-ray therapist now know what has or has not been achieved and what each may have to do to correct results.

The function of X-ray therapy.—It now seems necessary to explain the function of X-ray therapy. X-ray therapy must reach those sites not adequately treated by the radium. Of these sites, Taussig (1934), Leveuf (1931), Sampson (1907), and others have shown the pelvic wall to be the most important: yet it is bound to receive the smallest radium dose. This region must, therefore, be the chief concern of the X-ray therapist especially for Stages III and IV.

In most hospitals the X-ray fields are put on symmetrically about the mid-line. To avoid overdosage to the parts treated by radium, one of the two following methods is usually adopted; in (a) two separate fields are positioned at a fixed distance from the mid-line as suggested by Quimby and Arneson (1935), or (b) a single large field is used with a lead strip over the centre of the applicator so that the middle of the field is cut out—the so-called "shadow" technique. Neither of these techniques takes account of the following considerations:

(i) The techniques are rigidly symmetrical about the mid-line whereas the radium lethal isodose level may be symmetrical but not about the mid-line or may not be symmetrical in any plane.

(ii) The most penetrating portion of each beam, i.e. the central rays, are not necessarily being used at the pelvic wall where the need is greatest.

(iii) The distance of the pelvic wall from the radium lethal isodose surface is not a fixed quantity.

(iv) The dose distribution in space of the "shadow technique" has not yet been agreed upon.

These points may be illustrated as follows:

The average pelvic wall is about 5 cm. from the mid-line. If a narrow beam is used, say 6 cm. wide, and centred with its edge 2 cm. from the mid-line, the plane of maximal dose will not include the glands of the pelvic wall but will be mesial to it. If large fields are used, say 10 cm. wide (as suggested by Quimby) placed 2 cm. from the mid-line, then the plane of maximal dose falls *outside* the pelvic wall. Since the pelvic wall is the site of the pelvic glands and the radium contribution is here at its lowest it is clear that the maximal X-ray distribution should be centred over the sagittal plane through the pelvic wall and not in relation to the mid-line sagittal plane. The width of the field to be used depends on the volume of the tissue between the pelvic wall and the radium lethal isodose surface. This zone of tissue will be referred to as the "radium para-lethal volume" and is often unequal on the two sides of the pelvis.

Fig. 9 shows an actual case taken from fig. 6a where the isodose surface is neither symmetrical in distribution nor equally disposed about the mid-line. If it be assumed that it is, and the right and left X-ray fields are put on symmetrically (fig. 9) then the right side will get an overdose and left side an underdose. If full account is taken of these inequalities, then the fields must be varied for each side of the pelvis.

Practical aspects of planning.—The above considerations indicate that a clear conception of the spatial relations of the zones to be irradiated is essential. To assist in visualizing the volume to be treated and the distribution required a wax impression of the true pelvis was taken from a skeleton. The hole in the centre represents the volume treated by a box and tube at 45° in the coronal plane. The two lateral slices of wax represent roughly the shape of the volume to be treated by X-rays—these are the "radium para-lethal zones".

All X-radiation missing this volume will be wasted and even dangerous. If mesial to it will be superimposed on parts already adequately irradiated by the radium. This explains those cases with apparent complete primary regression which later develop symptoms of renal dysfunction, due to compression of the ureter as a late radiation phenomenon. In America ureteric dilatation has for this reason been urged for all radium-treated cases by Hoffmann (1942) and others. It is most important that a

pre-radiation pyclogram should be done as a standard for comparison later. Probably the same explanation of spots of high dosage accounts for the delayed radiation reactions in the rectum described by the late T. F. Todd (1938).

If lateral to this volume the radiation will fall outside the true pelvis lowering the limit of efficient radiation and damaging normal tissues.

In certain cases even necrosis has been produced such as those reported in the femoral neck (Strauss *et al.*, Dalby *et al.*). The cause is well shown by the position of the high dosage area in fig. 10.

The "Para-lethal Zone" will already have received some radiation, at least of the order of 1,000 to 2,000 r, from the radium. This must be added to the dose from the other X-ray fields. The problem of addition of X and γ radiations is complex. 1,000 r given by X-ray does not produce the same biological effect as 1,000 r from radium. It will suffice to say here that the ratio 1 to 1.6 suggested by Garcia (1943) seems likely. During the interval between the first radium insertion and the X-ray therapy in addition to tumour regression both distortion and dislocation of pelvic structures may take place. Tissues already irradiated by the radium may thus be pulled into new positions by the time X-ray therapy begins. Allowance must be made for this.

The problems set for the X-ray therapist should now be clear. He cannot plan his radiation until he knows what has been delivered by the radium. Guessing and the use of a standard X-ray technique may lead to over- or under-dosage as explained. Hence the failure at certain clinics to obtain any improvement by the addition of X-ray therapy to their existing radium techniques, and the reason for some disasters. This in my view is because such X-ray techniques had not been planned to fit in with the individual radium distributions. Their adverse results are a criticism of the combination of a routine X-ray technique with a radium treatment of unknown volume distribution. It is unjustifiable to condemn X-ray therapy on such evidence. The X-ray technique must be planned to fit the individual radium distribution. There seem to me to be no scientific reasons even if there are good administrative ones for restricting X-ray therapy to Stage III and IV cases only. As already stated, many Stage I and II cases have already microscopic evidence of lymph-node invasion. The case against planned X-ray therapy for all stages of cancer as advocated here, has yet to be proved.

Radium should not be inserted by one person and X-rays offered by another, each being unaware of the volume dosage delivered by the other. Worse still is the practice whereby the X-ray therapist never sees the patient at all after her radium treatment unless she returns with a recurrence. To utilize X-rays as a placebo in this way is defeatist folly which must rob many of their chance of survival. Radiotherapy in the pelvis should be one treatment, planned as a combined operation, even if the two parts of it are administered by different individuals.

For those portions of the work beyond the scope of the gynaecologist the necessary technicians must be provided. If it be argued that there is not enough time to do such methods one could reply that a Wertheim operation, too, could be speeded up by not removing the lymph nodes! If a method is recognized as inadequate ought we to continue doing many such inadequate treatments, or increase our staff and do the treatment adequately?

Scheme for treatment.—The fullest co-operation between gynaecologist and X-ray therapist should be undertaken before any treatment is given. The latter should certainly study gynaecology and it is not too much to say that all who handle radium should know something of the physics and biological actions of radiations and of the dangers both to the patient and to the operator.

(1) Before the insertion of the radium every means must be taken to ascertain the limits of the primary and the extent of the spread by palpation, colposcopy, cystoscopy, proctoscopy and pyclography. These five procedures should be routine. Davis and others have also utilized hysterography, Sante pneumoperitoneum and Farinas arteriography in an attempt to localize tumour spread. Both therapist and gynaecologist should be present or have made available to them the results of these examinations.

(2) After a full clinical assessment of the patient the treatment plan must be decided upon, e.g. it has been our practice sometimes if the tumour is very large to give a portion of the X-ray dosage first in order to secure partial regression of the tumour. This permits later on a much better situation than would have been possible with a bulky tumour filling the vag. times direct application by contact X-rays *per vaginam* has been attempted. Questions of this type must be decided at a joint consultation given. Such questions as lymph node to be decided at that time. would be taken

(3) The radium ha

would be taken

a) to check the correctness of the insertion, and (b) as a record for dose estimation. It will already have been decided by joint discussion what type of applicators to use and the dose to be given. The basal-plane already described (Sandler, 1943) is used for recording the radium position.

(4) Variations in the positions of the radium during treatment must be investigated and the dose distribution analysed. This may require the services of a full-time technician.

Since physicists are employed by most hospitals to check the dose distributions of radium applicators used for other organs of the body there is no reason why such work should not be extended to the cervix.

(5) Serial biopsies for cytological analysis and guidance for dosage should be undertaken in co-operation with a cytologist.

It is fully realized that no revolutionary techniques have been described so far. Nevertheless it is hoped that by a better understanding of the methods we are using at present we may still be able to improve our results with this dreadful disease.

In conclusion I have to record my thanks to the Director of the Radiotherapy Department, Dr. D. W. Smithers, to Mr. D. MacLeod, F.R.C.S., Mr. J. B. Blaikley, F.R.C.S., and Dr. M. Lederman for facilities to treat cases. I also wish to thank Professor W. V. Mayneord and Dr. P. C. Koller, Ph.D., D.Sc., for the loan and preparation of photographs.

[Many illustrations have had to be omitted for lack of space.]

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Dr. P. C. Koller: Cytological analysis of different tumours in various tissues indicates that radiotherapy must take into consideration the biological activity of tumour cells and tissue in the planning of the treatment. Our investigations, carried out in the Royal Cancer Hospital, have definitely shown that tumours differ in this respect and therefore they should not all be treated in the same way. The two kinds of radiation effects, one which concerns the individual cells (intracellular reaction), and the other which occurs in the tumour tissue (intercellular response) can be used more economically if the biological activity of the tumour is known.

Dr. Malcolm Donaldson agreed with Mr. Sandler that there were two problems in the radiotherapeutic treatment of carcinoma of the cervix: (1) The physical; (2) the biological. Of these he thought the first would be more easily solved, and mentioned that Dr. Neary had published a paper on a new radium container which it was hoped would give a much more even distribution than was at present obtainable (*Brit. J. Radiol.*, 1943, **16**, 225).

The Effect of Deep X-rays on the Peritoneal Metastases of an Ovarian Carcinoma.—
 JAMES WYATT, F.R.C.S.

Mrs. A. M. H.; one child aged 11. Admitted 1.9.43 with a history of lower abdominal pain for three weeks.

History.—A fairly sudden attack of lower abdominal pain, colicky in nature. No relation to food or to micturition or defecation; the pain did not radiate and there was no sickness.

Abdominal examination.—There was a mass rising from the pelvis almost to the umbilicus; it was firm and did not appear to be fixed.

September 9, 1943, laparotomy was performed. The peritoneal cavity contained some free fluid and there were secondary growths in both the walls of the cavity and the omentum; the pelvis contained a mass of growth appearing to arise from the left ovary, spreading directly on to the pelvic colon. A piece of omentum containing a secondary nodule was removed for biopsy and showed secondary deposit of a spheroidal-celled carcinoma.

A course of deep X-ray therapy was given covering the whole peritoneal cavity.

She was seen in October and December 1943; and in March 1944 her general health was good and she was putting on weight. In March, on abdominal examination, no abnormal swellings could be detected.

In August 1944 she was found to have a cystic swelling rising out of the pelvis to just above the umbilicus. She was therefore readmitted, and under an anaesthetic the tumour appeared quite smooth and mobile; so the abdomen was again opened.

There was no sign of any secondary deposits in the peritoneal cavity, the cystic swelling which arose from the left ovary was not adherent, and the surface was smooth with a few small injected areas similar to those appearing on the skin after deep X-ray therapy.

The tumour was removed, and as the right ovary appeared absolutely normal it was left in situ.

Convalescence was normal.

On opening the cyst it was found to contain a straw-coloured fluid and there were a number of raised nodules on the inner wall, appearing rather necrotic. Section of one of these masses showed the appearance of a papilliferous carcinoma with large areas of necrosis present.

This case suggests that the deep X-ray therapy destroyed the metastatic growths in the peritoneal cavity and the growth on the surface of the ovary but was not sufficient to destroy the intracystic growth, which after an interval started to develop again and would later have disseminated. Therefore it would appear that, following deep X-ray therapy in those cases where it is impossible to remove the parent tumour, if the physical signs show marked retrogression of the growth, the abdomen should be opened to see if a radical operation can be performed.

An Unusual Case of Carcinoma of the Ovaries.—RALPH WINTERTON, F.R.C.S.

Mrs. D. T., aged 26. First came up to the Hospital for Women in August of 1941 complaining of sterility. She was married two years and her periods were $\frac{8-4}{28}$.

On examination.—An abdominal swelling was felt and she was admitted for operation. At laparotomy she was found to have bilateral ovarian tumours measuring 5 in. by 4 in. and 4 in. by 4 in. These were solid, and though the capsules appeared intact a diagnosis of bilateral carcinoma of the ovaries was made. There were no secondary deposits seen.

It was felt that if these tumours were malignant the prognosis was hopeless whatever treatment was employed and one has a prejudice against removing both ovaries when a patient's primary complaint is sterility. Therefore portions of both ovaries were left as it was felt that though her life might be shortened by a few months, it would be happier while it lasted.

The section of the ovary shows: "Papillary adenocarcinoma with solid areas of spheroidal cells."

The patient was seen at intervals after that; on each occasion she was fit; periods $\frac{3-4}{28}$ and she was still worried about sterility.

In March 1943 on examination under anaesthetic the pelvis appeared normal and a biopsy of endometrium was taken which again showed carcinoma.

There was now no alternative but to do a hysterectomy (April 14, 1943). On opening the abdomen the ovaries appeared perfectly normal. She had a total hysterectomy and the ovaries were again conserved.

Microscopically, the uterus appeared healthy except for a thickened area of endometrium just above the cervix. Section of this showed an area of adenocarcinoma in which were solid masses of cells with numerous mitoses. The rest of the endometrium appeared healthy.

She is still alive and well eighteen months after the hysterectomy. Six months ago she stated that she had adopted a child.

Section of Surgery

President—Sir JAMES WALTON, K.C.V.O., M.S.

[December 6, 1944]

Torsion of the Great Omentum: Report on Four Cases

By W. ETHERINGTON-WILSON, F.R.C.S. [*Abstract*]

THE great omentum may twist as a whole, or as a part or strand: either twist may be complete (strangulated) or incomplete (congested) and may be primary or secondary. Primary twists are necessarily intra-abdominal and unipolar and no definite cause can be assigned. Secondary rotation cases may be uni- or bi-polar; a hernia, adhesion, cause for ommental deformity, or evidence of past or present intraperitoneal inflammation, being present. The omentum may be entirely intra-abdominal, wholly in a hernial sac, or there may be combined hernial and abdominal rotation. The condition may be acute or subacute, and there are probably recurrent cases.

Of all varieties some 190 cases are recorded in the literature.

Causation.—Though still speculative, it does appear that a combination of factors are responsible, some predisposing (peristaltic pushes by the muscle of the intestines, abdominal wall and diaphragm); sudden jerky body actions and rotations; direct blows; ommental disfigurement by tumours, overloading or uneven fat distribution, pedicle formation, scarring, raggedness, adhesions and bipolar attachments: displacement of the omentum during operation or by abdominal tumours. A history of one or more of these conditions is found among the cases recorded.

A partial twist having started and caused congestion of the veins with œdema, it has been suggested (Payr) that the shorter and firmer arteries may complete the process. Any other condition producing œdema of the omentum, i.e. the heart or adjacent peritoneal inflammation might produce the same result.

Diagnosis.—Typically, the patient aged 30 to 55 years complains of right-sided, gradually increasing, spasmodic pain, often relieved by lying down. 80% are considered to be appendicitis, yet tenderness, rigidity, distension and the signs of a toxic state are absent. Palpation of a doughy tumour is suggestive. The prognosis is good.

Operation.—The procedure as in all cases of torsion is obvious. The earlier the exploration the fewer the regrets. In such doubtful diagnoses the gridiron incision should not be used. The omentum or a part is almost always removed. In Case III, for reasons given, I untwisted what was probably an unstrangulated omentum for the sake of speed, the patient dying from thyrotoxic effects in a few hours. In Case IV I believe I was justified in not embarking on the removal of the whole of a huge omentum, though I did not know at operation that it was infected by early tuberculosis. The patient recovered. Thus one case died out of four and this an omentum which was least affected by strangulation judging by its colour; death was due to thyrotoxic cardiac failure.

When the rotated omentum is removed it should be examined with care and a note made of any tumour, pedicle formation, fibrosis or deformity present. The maximum narrowing or pedicle formation has been noted as being present in any part of the specimens removed. Cases I and II were constricted above near the colon. Case III had a narrowing 3 in. from the lower end just above the consolidation; in Case IV, no narrowing was present. Case II was an excellent example of a peg top, the adhesion below being firm, thick and pointed. There may be few or numerous twists, clockwise or anti-clockwise.

SUMMARY

- (1) An account has been given of intra-abdominal torsion of the *great omentum*.
- (2) The diagnosis and aetiology has been discussed.
- (3) Four personal cases have been presented.
- (4) The specimens were shown at the Section of Surgery, Royal Society of Medicine, on December 6, 1944, and have been accepted by the Royal College of Surgeons' Museum, London. They represent axial rotation of the whole omentum intra-abdominally, Case I being a primary, Cases II, III, and IV, secondary torsions.
- (5) Too many cases are being recorded of twists of a small gastrocolic strip or tag, among the collection labelled omental torsion. A separate group should include the more important torsion of the whole great omentum.
- (6) An extensive and critical survey of all cases and previous reports, up to 1944, brings the total cases to about 190, of which 38%, or 73 cases are idiopathic.

Appendicitis in the Newborn. Report on Case 16 Days Old

By W. ETHERINGTON-WILSON, F.R.C.S.

ACUTE appendicitis in the very young is rarely seen. By the newborn is meant babies a few hours or days or a very few weeks old.

From the reports (Emerson, 1943, and Abt, 1917) by Beckman, Allen, Potts, Hudson, Chamberlain, Busch and others, the appendix cases in children up to 12 years of age number 2,988 and only six of these were found to be one year old or under. Abt lists 80 infants with appendicitis from 1847 to 1917: of these 37 were one year old or less. Holman (1938) reported no child under 2 years of age in 1,200 cases. In 500 consecutive personal cases of appendicitis, that here reported is the only one under 2 years of age. Many such series can be found in the literature and all serve to prove the greater rarity of appendicitis in the very young, or newly born.

In a survey of the literature the following cases have been noted: Cases from 4 to 32 weeks number 32: of these 6 were in hernial sacs; 26 were true intra-abdominal cases; 23 males, 6 females, 14 recovered, 13 died; only 5 of the cases were 4 to 6 weeks old.

A younger group still, *under 4 weeks*, produced 15 cases: 6 were in hernial sacs with 9 true intra-abdominal appendices: 8 males, 4 females: 6 recovered, 9 died. My case is included. Four of these were accounted prenatal. All 6 recoveries were hernial cases.

Four cases of so-called prenatal appendicitis are included above and are reported by Jackson, Hill and Masson, Corcoran and Kümmell. All were dead by the third day. Apart from these early prenatal cases and those found in umbilical and scrotal hernial sacs, the straightforward intra-abdominal acute appendix has been met with in babies, 5, 14, 16 (my case), and 21 days old (two cases), a total of five cases.

Case report: Baby (A), male, birth-weight 3½ lb., premature, induced labour, first child, born in November 1944 at the Torbay Hospital, Torquay. Well and thriving till 14th day when reported to be off feeds, vomiting, apparently in pain and with a rise in temperature. The condition progressed till I saw him on the 16th day, 9 p.m. The condition appeared grave with pinched facies and signs of dehydration; vomiting in clear, small amounts continued; constipation, abdomen very distended, tympanitic and tender all over; temperature not raised and pulse difficult to count. Much weight had been lost. The appearances suggested a poor surgical risk, yet the cry was strong and it was felt that infusions would help. An exact diagnosis was not made, though peritonitis suspected. By 11 p.m. the same night the operation had been completed after considerable improvement following 20 c.c. subcutaneous rapid infusions and an intra-tibial drip, which gave 100 c.c. in two hours. Operation was performed under perfect controlled spinal analgesia by my technique. 1½ c.c. 1:2,000 hypobaric nupercaine was injected in the vertical position, twenty seconds allowed for ascent. Tested analgesia showed a block to the ensiform cartilage. No anxiety was given at any time. Confronted with a retro-caecal appendix, an immobile caecum, diffuse peritonitis, and worst of all an incision placed too high for a difficult appendicectomy, it was considered unjustifiable to enlarge the right paramedial incision. The pelvis was drained and the wound carefully sutured. The child's condition improved out of all recognition for twelve hours, mostly due to the compensated dehydration probably. Death took place forty-eight hours later. It is possible that this is the youngest and smallest (weight ? 3 lb. 4 oz.) baby to have a spinal anæsthetic, and is certainly the least of my series of cases. The specimen was removed post mortem. At a posterior view of the caecum, ileum and appendix: the distal half of the is sharply defined and gangrenous, the proximal half almost normal. No concretion seen. Adenitis of lymph and enlarged lymph nodes are visible. [The specimen was at the Royal College of Surgeons.] and has been presented to the Museum of the Royal College

Diagnosis.—Acute appendicitis in newborn and very young infants may occur intra-abdominally in the pre- or post-natal periods, and has been found in hernial sacs. Male cases seem much more common than female. Diagnosis, so imperative to be early, is often late with fatal results. The condition in most cases gives rise rapidly to peritonitis and localization in the abdomen is uncommon: gangrene appears to be the rule. Diagnosis at a very early stage; however, is difficult for obvious reasons of age and rarity.

Refusal to feed adequately, vomiting, persistent crying, constipation in most cases, pyrexia and a raised white count should lead to a careful, repeated, unhurried, examination of the abdomen and suspicion should be aroused if the most important sign of peritoneal tenderness can be definitely ascertained in the right lower quadrant (under the best of warm conditions), a local thickening should be carefully felt for, it is reported in some cases. The same sign is of significance if felt *per rectum*. Diarrhoea and melena have been reported in the old cases to assist in deception and many other conditions have been suspected in error.

Treatment.—For operation I am convinced about the efficacy of spinal analgesia when given with full knowledge and care. Pre- and post-operative infusion is invaluable to lessen operative or immediate post-operative fatality. Early operation should produce about 60% of recoveries. Under 4 weeks all unoperated cases have died: the prognosis in hernial appendicitis is good—100%: in the same group the intra-abdominal case prognosis is as bad as possible, the percentage of recoveries rising in the older infants.

SUMMARY

- (1) An account is given of appendicitis in infancy.
- (2) Early post-natal appendicitis is rare—very fatal under 4 weeks of age, less so as age advances.
- (3) A case of appendicitis beginning on the fourteenth day with operation on the sixteenth day is recorded.

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The following specimens were shown:

- Mr. J. S. R. GOLDING (for Mr. R. VAUGHAN HUDSON): (1) Cavernous Lymphangioma of the Spleen. (2) Pancreatic Cyst and Chronic Pancreatitis—Pancreatic Calculi in the Pancreatic Duct.
- Mr. H. A. KIDD: Retroperitoneal Tumour.
- Mr. REGINALD T. PAYNE: Adenolymphoma of Parotid.
- Mr. D. RANGER (for Mr. R. VAUGHAN HUDSON): Hydatid Cyst of the Liver.
- Mr. D. RANGER: Strangulation of Pelvic Colon.
- Sir JAMES WALTON, K.C.V.O.: (1) Hour-glass Gall-bladder with Different Stones in Each Portion. (2) Stone in Common Duct (Overlooked Stone). (3) Pure Calcium Carbonate Stones. (4) Pure Calcium Mass with Laminated Stones. (5) Intramural Stones. (6) Stones Around Sutures. (7) Recurrent Stones in Gall-bladder.
- Mr. A. DICKSON WRIGHT: (1) Jejunal Ulcer Following Devine Exclusion. (2) Volvulus of the Gall-bladder.

[January 3, 1945]

DISCUSSION ON DIAGNOSIS AND TREATMENT OF *B. COLI* PYELITIS

Mr. E. W. Riches: This discussion includes *B. coli* pyelitis of adults, pyelitis of infancy, and special varieties such as pyelitis of pregnancy; I shall deal mainly with the disease as it affects adults.

There are two main clinical varieties, acute or subacute, and recurrent. The so-called chronic pyelitis is always a pyelonephritis with tubular involvement, and even the name recurrent pyelitis usually conceals some other lesion which is responsible for stasis, atony or trauma in the urinary tract.

The two principal aetiological factors are a lowered resistance, and bacterial invasion. The lowered resistance is exemplified by the frequent occurrence of a chill, exposure to cold, or excessive alcohol before the attack starts. The bacterial invasion is generally from the bowel, a preceding constipation or diarrhoea giving the clue to its origin, and the infection is usually lymph-borne from the colon. Ascending infection from the bladder by peri-ureteral lymphatics or possibly by the lumen of a dilated ureter is another route, and occasionally a haematogenous infection may occur from some other septic focus in the body. The origin from the bladder is suggested when the symptoms of cystitis precede those of renal infection, although it seems impossible to have renal without bladder infection and the term pyelocystitis or cystopyelitis is preferable. Indeed the distinction between pyelitis and cystitis is a somewhat arbitrary one; if pyrexia or renal pain occurs in a patient with cystitis the label pyelitis is attached; catheterization of the ureter is contra-indicated in an acute case, but where it has been done a high proportion of the cases show a sterile kidney urine.

The symptoms in the acute phase are well known; pyrexia sometimes with a rigor, nausea or vomiting, a renal ache, polyuria, frequency and dysuria, and rarely slight but painful haematuria if the accompanying trigonitis is severe. The urine is characteristically acid, pale, of low specific gravity with an unpleasant odour and a surface sheen which develops on standing. The finding of pus and *B. coli* in the urine is the only confirmatory investigation required, and a response to proper medical treatment is evidence of the correctness of the diagnosis. Fuller investigations are reserved for persistent or recurrent cases. The differential diagnosis from acute appendicitis or salpingitis is made on the site of the tenderness and the presence of pus and *B. coli* in the urine, although appendicitis and pyelitis may coexist.

The treatment of the acute case consists of rest in bed, with warmth, copious fluids, attention to the bowels and the administration of alkalis in sufficient doses to make the urine alkaline. This may mean up to two drachms of potassium or sodium citrate two-hourly. When the temperature has been normal for a few days a further bacteriological examination of the urine is made and the continued presence of *B. coli* or of pus demands a course of either one of the sulphonamides or of mandelic acid. Sulphonamides are quicker in their sterilizing effects, taking about half the time of mandelates; a high fluid intake and alkalis are maintained and the danger of sulphonamide anuria is then minimal. The drugs are not always well tolerated, and may produce nausea and vomiting if given in adequate doses. Efficiency and toleration seem best combined in sulphadiazine for this infection. Mandelic acid is best given as calcium or ammonium mandelate; fluid intake must be restricted to two pints daily and a full dose of the preparation equivalent to 3 g. of mandelic acid must be taken four times a day for ten to fourteen days. The urine should reach an acidity of pH 5.3; if it does not ammonium chloride must be given.

For a pure *B. coli* infection I find mandelic acid more generally useful than sulphonamides although it too is unpleasant to take. It can safely be given to an ambulant patient. For the speediest cure, however, sulphonamides should be given with alkalis from the outset. If the case fails to clear up under one of these measures it is probably not one of uncomplicated pyelitis.

In the diagnosis of the recurrent or persistent case, search must be made for the ultimate cause of the stasis, atony or trauma which keeps up the infection. It may lie in the urinary tract itself, or in the genital or intestinal tract. Once found it must be removed or corrected; and the infection treated. As the lesion is most commonly found in the urinary tract investigations should as a rule start there, and the most useful starting point is an intravenous pyelogram. I prefer to do that before cystoscopy; it may indicate or obviate the need for an instrumental pyelogram and thus save the patient a second cystoscopy. A plain X-ray of the urinary tract rarely gives enough information upon which to act; even if stones are found the full extent of the lesion is only revealed by the excretion urogram.

The next investigation is cystoscopy, which is preferably deferred until the acute symptoms have abated. Any lower urinary tract obstruction will be discovered at this examination if not before, and any lesion in the bladder such as a new growth, diverticulum, stone or ureterocele. The extent and degree of cystitis can be ascertained and recorded for future comparison. The ureters can be catheterized for diagnostic purposes and this may also have some beneficial therapeutic effect in certain cases. Retrograde pyelography is done at the same time if the previous excretion pyelogram indicates the need; this will arise where there is no secretion from one kidney, or where the intravenous pictures are not sufficiently clear for diagnosis. I will cite a few examples of various conditions revealed by one or other of these diagnostic methods; all these patients presented as cases of pyelitis with a *B. coli* urinary infection. They will give an indication of the various types of surgical treatment adopted before the infection could be controlled.

Hydronephrosis of varying degree is perhaps the commonest lesion disclosed. A woman of 34 had a persistent infection with a right-sided pain for eight years which had failed to respond to the usual measures and to a course of renal lavage; exploration showed no obstructive cause for the hydronephrosis and renal sympathectomy was performed; sixteen months later the kidney was still dilated but the urine was sterile and remained so when she was seen over four years later. Other procedures which may be required are nephropexy; division of aberrant vessels and plastic operations. One illustrative case of the last mentioned may be given:

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Another unusual cause, but one which may give rise to difficulty in diagnosis is a non-opaque calculus. A girl of 15 had recurrent attacks of so-called pyelitis with occasional hæmaturia; intravenous pyelography appeared normal, but the retrograde pyelogram showed a circular negative shadow in the pelvis; it was a urate stone, which was removed, and the attacks ceased.

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The lower urinary tract and the genital tract must also be investigated; in the male chronic prostatitis is sometimes found as the primary lesion, and in the female the cervix may contain an erosion. The urethroscope is needed in some cases of congenital urethral valve, both for diagnosis and treatment. Congenital abnormalities frequently lead to dilatation and stasis, conditions which predispose to persistent investigation. Horse-shoe kidney is an example where the faulty drainage is sometimes amenable to surgical correction. Renal reduplication is another. In one case the lower half of the left kidney was a pyonephrotic sac; it was treated by heminephrectomy.

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The two principal aetiological factors are a lowered resistance, and bacterial invasion. The lowered resistance is exemplified by the frequent occurrence of a chill, exposure to cold, or excessive alcohol before the attack starts. The bacterial invasion is generally from the bowel, a preceding constipation or diarrhoea giving the clue to its origin, and the infection is usually lymph-borne from the colon. Ascending infection from the bladder by peri-ureteral lymphatics or possibly by the lumen of a dilated ureter is another route, and occasionally a haematogenous infection may occur from some other septic focus in the body. The origin from the bladder is suggested when the symptoms of cystitis precede those of renal infection, although it seems impossible to have renal without bladder infection and the term pyelocystitis or cystopyelitis is preferable. Indeed the distinction between pyelitis and cystitis is a somewhat arbitrary one; if pyrexia or renal pain occurs in a patient with cystitis the label pyelitis is attached; catheterization of the ureter is contra-indicated in an acute case, but where it has been done a high proportion of the cases show a sterile kidney urine.

The symptoms in the acute phase are well known; pyrexia sometimes with a rigor, nausea or vomiting, a renal ache, polyuria, frequency and dysuria, and rarely slight but painful haematuria if the accompanying trigonitis is severe. The urine is characteristically acid, pale, of low specific gravity with an unpleasant odour and a surface sheen which develops on standing. The finding of pus and *B. coli* in the urine is the only confirmatory investigation required, and a response to proper medical treatment is evidence of the correctness of the diagnosis. Fuller investigations are reserved for persistent or recurrent cases. The differential diagnosis from acute appendicitis or salpingitis is made on the site of the tenderness and the presence of pus and *B. coli* in the urine, although appendicitis and pyelitis may coexist.

The treatment of the acute case consists of rest in bed, with warmth, copious fluids, attention to the bowels and the administration of alkalis in sufficient doses to make the urine alkaline. This may mean up to two drachms of potassium or sodium citrate two-hourly. When the temperature has been normal for a few days a further bacteriological examination of the urine is made and the continued presence of *B. coli* or of pus demands a course of either one of the sulphonamides or of mandelic acid. Sulphonamides are quicker in their sterilizing effects, taking about half the time of mandelates; a high fluid intake and alkalis are maintained and the danger of sulphonamide anuria is then minimal. The drugs are not always well tolerated, and may produce nausea and vomiting if given in adequate doses. Efficiency and toleration seem best combined in sulphadiazine for this infection. Mandelic acid is best given as calcium or ammonium mandelate: fluid intake must be restricted to two pints daily and a full dose of the preparation equivalent to 3 g. of mandelic acid must be taken four times a day for ten to fourteen days. The urine should reach an acidity of pH 5.3; if it does not ammonium chloride must be given.

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specimen that has been thoroughly shaken. The urine from a male child, obtained after cleaning the penis, and examined in this way, should be free of pus, but in a girl, even in the absence of any demonstrable vulvitis, one or two pus cells may be found in each field under a $1/6$ power of the microscope, and therefore a number of cells per field in excess of this is required before the diagnosis of pyelitis is made. If the finding of pus in the urine is the principal criterion in the diagnosis of pyelitis, then a catheter specimen is not strictly necessary, or perhaps it would be better to say that it is unnecessary to wait upon a catheter specimen before making the diagnosis. A catheter specimen is only necessary if culture of the urine is contemplated, but in practice it is a great advantage to know the infecting organism, as this knowledge may determine the type of treatment to be undertaken. In a male child, a non-catheter specimen of urine obtained after careful cleaning of the penis, and the rejection of the first few drops of urine, will usually suffice for culture, but in a female infant a catheter specimen must be insisted upon if culture is intended. The culture of bacilli from a "clean" but non-catheter specimen of urine from a girl is of no clinical significance.

The amount of pus varies also from day to day. When the temperature is high pus may be absent from the urine, and then with a sudden fall in the fever a gush of pus appears in the next specimen, as though the temperature had been associated with pus pent up in the renal pelvis or in an unerupted abscess within the kidney substance. When pus is plentiful it is common for the cells to clump together in batches of 100 or more.

As to other changes in the urine, the output is usually diminished until treatment has had time to take effect. The reaction (in *B. coli* pyelitis) is strongly acid. Albumin is present in amounts comparable with the amount of pus, but examination for albumin is of no importance as a means of diagnosis. Blood cells are also often present, although seldom sufficient to discolour the urine. Casts, especially hyaline and granular, may also be present, depending on the degree of renal involvement, and epithelial cells from the urinary tract are often plentiful.

Differential diagnosis.—Various conditions may be mistaken for pyelitis. Irritability, vomiting and constipation in a young child form a triad of symptoms always calling to mind tuberculous meningitis, while the signs of meningism that may occur in pyelitis may suggest some more acute form of meningitis. In infants the vomiting and passage of loose stools may make the picture of gastro-enteritis so prominent that the possibility of pyelitis may at first be overlooked. In older children, tenderness over the right side of the abdomen and some guarding of the muscles may simulate appendicitis. It must suffice to say that errors of diagnosis will continue to be made so long as a routine examination of the urine is omitted from the clinical examination.

Treatment.—Before the advent of sulphonamides, acute *B. coli* pyelitis was treated with alkalis, usually with conspicuous success. Provided the alkaline treatment was efficiently carried out, failure to achieve cure was usually an indication of the presence of urinary stasis, and in children such stasis is almost always due to some congenital abnormality of the urinary tract. Hence a failure of alkaline treatment was an indication for further investigation of the urinary passages by such means as intravenous pyelography, and cystoscopy with retrograde pyelography. Harmful effects from the alkalis were seldom met with, although in infants they would occasionally cause a temporary œdema, or promote looseness of the stools.

The sulphonamides are such efficient sterilizers of the urine, that they will often exert this effect in the face of urinary stasis. If these drugs are used as a routine in acute pyelitis, the child is afforded no opportunity of indicating whether urinary stasis is present, nor whether pyelographic investigation is really necessary. It follows that if these drugs are used as the first line of attack in acute pyelitis, successful treatment should be followed by a routine pyelography in case some underlying cause of urinary stasis be overlooked. My personal opinion is that this is not fair to the children. Moreover sulphonamides, as is well known, are capable of exerting toxic effects. It is therefore my practice to continue to treat acute *B. coli* pyelitis by alkalis: if this fails, to turn to sulphonamides, and later on to investigate this group of children by pyelography.

Alkaline therapy.—The urine must be rendered alkaline as swiftly as possible, and its alkalinity maintained for two to three weeks. Either potassium citrate alone, or a combination of the citrates and bicarbonates of sodium and potassium may be used. For an infant gr. 10 two-hourly by day and three-hourly by night will suffice, for an older child the dose may be increased to gr. 20 or 30; simple fluids should also be pushed. Each specimen should be tested with litmus paper as soon as it is passed, and in an infant the litmus paper can be incorporated in the napkin. It is usually easy to reduce

save for some stasis on the right side, but the cæcum was found to be persistently in the pelvis and at operation the appendix, also lying in the bottom of the pelvis, was distended with pus at its tip which lay behind the bladder.

Other focal points of infection which should receive attention in obscure cases are the gall-bladder and the teeth and tonsils and sinuses. "Honeymoon pyelitis" requires sympathetic consideration and explanation, with treatment on medical and gynaecological lines.

To summarize, uncomplicated acute pyelitis due to *B. coli* will respond to medical measures; instrumentation plays little part in its treatment. The effective urinary antiseptics are mandelic acid and the sulphonamides. A case which does not respond to a properly given and supervised course of treatment should be regarded as having some other lesion which must be searched for and treated if the patient is to be cured. The persistence of pus cells after the urine has been sterilized is a warning that recurrence of infection is likely.

Dr. Wilfrid Sheldon: *Age.*—Although pyelitis occurs at any age it is most common in childhood and may be encountered within a few days of birth; indeed its incidence in childhood is greatest during the first year, after which it shows a considerable decline.

Sex.—Pyelitis is certainly much more common in the female in the case of children beyond the age of infancy, but at a time when the disease is most frequent, namely in the first year, the incidence in boys and girls is roughly equal, while in the neonatal period there is actually a preponderance in boys. The sex incidence in the first year, at a time when napkins are being worn, serves to throw doubt on the view that pyelitis is usually the outcome of an ascending infection, for at no age is the perineum so liable to heavy contamination as in infancy, and if ascending infection takes place more easily in the female than in the male, then pyelitis in infancy should be particularly a disease of girl babies. To teach that pyelitis is more common in girls calls for modification when speaking of infants, otherwise the possibility of pyelitis being the explanation of obscure fever and illness in boys may pass unsuspected, and the need to obtain a specimen of urine and examine it under a microscope for the presence of pus cells may be overlooked.

Relation to other diseases.—Although in many instances pyelitis appears to be a primary condition, it not infrequently arises in infancy as a secondary disorder. The most common predisposing illness is gastro-enteritis or some less severe disturbance of intestinal function such as the passage of loose curdy stools or constipation.

Symptoms.—In cases arising secondarily, the onset may be entirely masked, and the diagnosis be made only as a result of routine microscopy of the urine, or through failure of the primary disease to react favourably to treatment. In primary cases the onset is usually swift. The temperature rises quickly 4° or 5° , and thereafter tends to show a daily swing over 3° or 4° ; in young children there may be a burst of convulsions, and occasionally rigors may occur. Vomiting is almost invariable, and may persist throughout the acute phase, usually accompanied by anorexia. In young children restlessness and irritability are so pronounced as of themselves to prompt an examination of the urine, while the pallid complexion and worried expression compound a facies at once suggestive of the disease. The pallor should not be mistaken for anæmia, which is only present in cases of long standing, but examination of the blood will reveal a polymorphonuclear leucocytosis. At times the irritation of the nervous system may lead to a condition of meningismus, with stiffness of the neck and a positive Kernig's sign, so much so that examination of the cerebrospinal fluid may seem justified, although this may be rendered unnecessary if a preliminary examination of the urine is made. In older children irritability is likely to be replaced by headache and pain in the loins, and at this age there is usually frequency of micturition both by day and by night, while younger children may temporarily surrender their recently acquired clean habits.

Pain is not a prominent symptom, though older children may complain of a dull ache in one or other loin, and may be tender over the hypogastrium. Although owing to their irritability infants may seem tender almost everywhere, if the face is watched while the abdomen is palpated, the features may be seen to wince when slight pressure is applied to one or other loin. Occasionally infants also seem to experience bouts of intolerable pain, which they indicate by their sudden screams with a stiffened body and an anguished expression, and such attacks have been attributed to the passage of clots of pus down the ureters.

Diagnosis.—This turns on the microscopical examination of the urine for pus. Pathological laboratories usually report upon the urinary deposit obtained after centrifugalization, but many doctors possess a microscope but no centrifuge, and in my opinion it is preferable to examine a drop of uncentrifugalized urine taken from the middle of a

iliac artery. The left ureter is protected by the promontory of the sacrum and it is crossed by the sigmoid colon, peristalsis in which will necessarily lead to intermittent release of any pressure which might occur. In a pyelogram taken at the 20th to 24th week, the right ureter will, in most cases of normal pregnancy, be seen to be markedly dilated, the dilatation affecting both the pelvis and the calices, and ceasing abruptly at the pelvic brim. Any dilatation that is found below this point is the result of muscular atony occurring early in pregnancy and common to both ureters. Marked dilatation may or may not lead to stasis, but should stasis be present infection is likely to occur, for it is known that 7.5% at least of normal pregnant women have *B. coli* in their urine.

This atony which affects the ureteral muscle in pregnancy is thought to be due to the presence of progesterone which is known to have an inhibiting influence on all plain muscle—for example, intestinal distension is a constant feature in early pregnancy and not infrequently occurs in the pre-menstrual state. Oestrogen appears to have a similar effect on the urinary tract, for Harold Burrows has shown that administration of this substance to mice is followed by marked dilatation of the ureter and bladder. He believes the phenomenon to be due to interference with the neuromuscular mechanism of urination.

Ureteral dilatation may be present with large ovarian cysts and impacted pelvic fibromyomata, both ureters being equally affected. Inflammatory conditions in the pelvis—such as a cellulitis—may cause similar changes and chiefly affect the ureter on its particular side. Finally, infections of the cervix are, as Winsbury-White has pointed out, a frequent and important cause of urinary infection and unless borne in mind and eradicated may be often a cause of unexplained recurrent pyelitis.

Diagnosis.—Pyelitis of pregnancy may present itself with acute symptoms of which the most outstanding may be right-sided abdominal pain, with rigidity and great tenderness, and appendicitis may be closely simulated. In appendicitis the temperature is never so high and the tongue never so clean, and in pyelitis the pulse is in relation to the temperature and rigors are frequently present, while the point of maximum tenderness is situated posteriorly over the costo-vertebral angle. Direct examination of the urine for pus and organisms should settle the diagnosis. In late pregnancy the differential diagnosis may be even more difficult owing to the fact that the site of the appendix is abnormally raised by the enlarging uterus, and in cases of appendicitis there may be apparent tenderness over the kidney leading to a diagnosis of pyelitis. The greatest danger is that both these conditions may co-exist and an appendicitis be overlooked.

Another outstanding symptom may be vomiting which can be extremely severe, and it is not uncommon to see cases of this sort diagnosed as hyperemesis gravidarum especially when occurring in early pregnancy and without examination of the urine. On the other hand, should pyelitis occur in late pregnancy, a diagnosis of "albuminuria" has occasionally been submitted, but the absence of any rise in the blood-pressure should be sufficient to exclude this possibility.

Finally, in mild cases of pyelitis symptoms may consist only of pain in the small of the back and there may be no urinary symptoms whatever which would point to the true nature of the disease. The condition may be overlooked completely and the symptoms ascribed to lumbago or to the many ills that the flesh is heir to—especially in the pregnant woman. The microscopic examination of a drop of urine can make the diagnosis.

Treatment.—It was Meave Kenny who first introduced the sulphonamide drugs in the treatment of urinary infections and by so doing reduced the duration of the disease from fourteen days at least to an average of three days. Sulphanilamide is adequate for all *B. coli* infections, but sulphathiazole, sulphadiazine, and sulphamezathine are all equally effective and are often preferred. In using sulphathiazole, which is less soluble than sulphanilamide, an adequate fluid intake of not less than five pints *per diem* must always be given to prevent the drug crystallizing out in the tubules. Should the drug be administered in the puerperium it is noteworthy that sulphonamides are excreted in the milk but not in sufficient strength to upset the child.

Termination of pregnancy is very rarely called for. At the Jessop Hospital, Sheffield, where between 1,200 and 1,400 deliveries occur yearly, Mr. Eric Stacey informs me that in no case in the last three years has this procedure been necessary, and at the West Middlesex Hospital, Mr. Stern has performed this operation only three times in the last ten years, and one of these cases had only one kidney. The operation was necessary in only one of my cases—a woman 16 weeks pregnant with no previous history of urinary infections, who resisted all treatment including the sulphonamides and ureteral catheterization. Severe hæmaturia developed and the patient became profoundly toxic and her condition

the urine to neutral, but this will not suffice, enough alkali must be given to take the urine over to alkaline. When this point is reached the effect on the child is often dramatic, the fever subsiding and the irritability quickly passing away. Failure of alkaline therapy is shown not only by persistence of illness and pyuria, but also by the urine becoming offensive.

Sulphonamide therapy.—In *B. coli* pyelitis the concentration of sulphonamide in the urine required to render it sterile is about 50 mg. per 100 c.c. Although estimation of the urinary sulphonamide level are not essential as a routine procedure, they should always be carried out before assuming that any case has failed to respond to this group of drugs. In pyelitis, the concentration of these drugs in the urine is of more importance than the concentration in the blood, and the desired urinary level can usually be obtained with a dose which is less than that required for infections in other systems of the body. Different workers prefer different preparations; my preference in urinary infection is for sulphathiazole or sulphamezathine, both of which are in general well tolerated by children, and are less likely to irritate the urinary passages by crystallization than is sulphadiazine. The drug is administered every four hours throughout the twenty-four hours, giving 0.25 gram per dose in the first year, 0.5 g. from 1 to 5 years, and 0.75 g. from 5 to 10 years. This roughly corresponds to 0.2 g. per kilo body-weight per day. It is advantageous to give a small dose of alkali, such as 5 gr., with each dose in order to assist toleration. The benefit of the sulphonamides is usually apparent within forty-eight hours.

Chronic pyuria.—Chronic or recurrent *B. coli* infection of the urinary tract in children is almost always the result of urinary stasis, caused as a rule by some congenital deformity of the passages, but occasionally by a calculus. Urinary tract deformities are by no means uncommon, occurring in about 2.5% of all post-mortem examinations in children. Not only do they render *B. coli* infection more likely, but also make it more resistant to treatment.

Many deformities can be eradicated or corrected by surgical operation, which should then of course be undertaken. There is a smaller group in which both kidneys are involved, and may be so disorganized that surgery is not likely to be successful. There is also a group in which obstruction to the flow of urine is due to neuromuscular dysfunction rather than to anatomical abnormality. These latter groups must be dealt with medically, the object being to overcome and prevent infection. Obstruction may sometimes be considered to be due to muscular spasm, and favourable results have then been found to follow courses of pituitrin, although my own experience in these cases—admittedly a limited experience—has been disappointing.

The attempt to limit infection in chronic or recurrent cases by means of alkalis is quite useless, and although extensive trials have been made of hexamine, hexylresorcinol and similar urinary antiseptics, vaccines, and sera, they are mostly without effect. The sulphonamides are here the most useful group of drugs, and they are given in the manner described for acute pyelitis. If the history shows that recurrences are likely, once the infection has been overcome a much smaller maintenance dose of sulphonamide may be given over several months in order to prevent further relapses. According to the age of the child, a dose of 0.5 g. to 1 g. given in divided doses during the day may be sufficient for this purpose.

The sulphonamides have proved so successful in *B. coli* infections that sterilization of the urine by mandelic acid is seldom called for. If, however, there is any contra-indication to giving the sulphonamides, such as intolerance or leucopenia, calcium mandelate, or ammonium mandelate in the form of the elixir, may be used, giving a teaspoonful two to four times a day according to the age, together with sufficient ammonium phosphate to keep the pH of the urine down to 5.5, the urine being tested daily with methyl red. It should be pointed out that when the kidneys are considerably damaged, and their concentrating power diminished, they are more likely to attain a sufficient concentration of sulphonamide than they are of mandelic acid.

B. coli falls within the group of organisms insensitive to penicillin, and therefore the use of this drug in *B. coli* pyelitis is not likely to be beneficial.

Mr. Douglas MacLeod: Pyelitis associated with child-bearing is a comparatively common complication of pregnancy and is found to occur in about 1% of all pregnant women. First there is marked atony of the ureteral muscle which leads to dilatation, actual lengthening, and kinking of the ureter, which may show itself as early as the 10th week and at that time affects both ureters equally. Later in pregnancy pressure from the growing uterus begins to make itself felt and affects the right ureter more than the left. This is almost certainly due to the fact that the uterus leans towards the right side, and, in addition, the right ureter lies in a more exposed position as it crosses the common

iliac artery. The left ureter is protected by the promontory of the sacrum and it is crossed by the sigmoid colon, peristalsis in which will necessarily lead to intermittent release of any pressure which might occur. In a pyelogram taken at the 20th to 24th week, the right ureter will, in most cases of normal pregnancy, be seen to be markedly dilated, the dilatation affecting both the pelvis and the calices, and ceasing abruptly at the pelvic brim. Any dilatation that is found below this point is the result of muscular atony occurring early in pregnancy and common to both ureters. Marked dilatation may or may not lead to stasis, but should stasis be present infection is likely to occur, for it is known that 7.5%, at least of normal pregnant women have *B. coli* in their urine.

This atony which affects the ureteral muscle in pregnancy is thought to be due to the presence of progesterone which is known to have an inhibiting influence on all plain muscle—for example, intestinal distension is a constant feature in early pregnancy and not infrequently occurs in the pre-menstrual state. Oestrogen appears to have a similar effect on the urinary tract, for Harold Burrows has shown that administration of this substance to mice is followed by marked dilatation of the ureter and bladder. He believes the phenomenon to be due to interference with the neuromuscular mechanism of urination.

Ureteral dilatation may be present with large ovarian cysts and impacted pelvic fibromyomata, both ureters being equally affected. Inflammatory conditions in the pelvis—such as a cellulitis—may cause similar changes and chiefly affect the ureter on its particular side. Finally, infections of the cervix are, as Winsbury-White has pointed out, a frequent and important cause of urinary infection and unless borne in mind and eradicated may be often a cause of unexplained recurrent pyelitis.

Diagnosis.—Pyelitis of pregnancy may present itself with acute symptoms of which the most outstanding may be right-sided abdominal pain, with rigidity and great tenderness, and appendicitis may be closely simulated. In appendicitis the temperature is never so high and the tongue never so clean, and in pyelitis the pulse is in relation to the temperature and rigors are frequently present, while the point of maximum tenderness is situated posteriorly over the costo-vertebral angle. Direct examination of the urine for pus and organisms should settle the diagnosis. In late pregnancy the differential diagnosis may be even more difficult owing to the fact that the site of the appendix is abnormally raised by the enlarging uterus, and in cases of appendicitis there may be apparent tenderness over the kidney leading to a diagnosis of pyelitis. The greatest danger is that both these conditions may co-exist and an appendicitis be overlooked.

Another outstanding symptom may be vomiting which can be extremely severe, and it is not uncommon to see cases of this sort diagnosed as hyperemesis gravidarum especially when occurring in early pregnancy and without examination of the urine. On the other hand, should pyelitis occur in late pregnancy, a diagnosis of "albuminuria" has occasionally been submitted, but the absence of any rise in the blood-pressure should be sufficient to exclude this possibility.

Finally, in mild cases of pyelitis symptoms may consist only of pain in the small of the back and there may be no urinary symptoms whatever which would point to the true nature of the disease. The condition may be overlooked completely and the symptoms ascribed to lumbago or to the many ills that the flesh is heir to—especially in the pregnant woman. The microscopic examination of a drop of urine can make the diagnosis.

Treatment.—It was Meave Kenny who first introduced the sulphonamide drugs in the treatment of urinary infections and by so doing reduced the duration of the disease from fourteen days at least to an average of three days. Sulphanilamide is adequate for all *B. coli* infections, but sulphathiazole, sulphadiazine, and sulphamezathine are all equally effective and are often preferred. In using sulphathiazole, which is less soluble than sulphanilamide, an adequate fluid intake of not less than five pints *per diem* must always be given to prevent the drug crystallizing out in the tubules. Should the drug be administered in the puerperium it is noteworthy that sulphonamides are excreted in the milk but not in sufficient strength to upset the child.

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grave. The pregnancy was terminated by hysterotomy with a dramatic result for within three days she was perfectly well. It is difficult to believe that pressure of the uterus had so much effect so early in pregnancy, and the rapid improvement must be assumed to be due to the withdrawal of some hormone.

I have not discussed puerperal pyelitis; this is usually an ascending infection from a previous cystitis, and both kidneys are usually involved. Urinary infections, including pyelitis, are the commonest causes of puerperal pyrexia.

In my opinion the acute severe form of pyelitis in pregnancy is not nearly as common as is supposed. At Queen Charlotte's Hospital in 1939 there were only six cases among 1,819 deliveries, 0.3%, and at the Jessop, Mr. Stacey reports a similar figure.* Secondly, though pyelitis must always be uppermost in our minds when consulted by a pregnant woman complaining of abdominal pain, the possibility of an acute appendicitis is always present and a wrong diagnosis may cost the woman her life.

ACKNOWLEDGMENTS

I would like to acknowledge my indebtedness to Mr. Eric Stacey, Mr. D. Stern, and Mr. Erskine for supplying me with helpful information, and to Dr. Rohan Williams for the excellent radiological lantern slides.

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 WINSBURY-WHITE, H. P. (1933) *Brit. J. Urol.*, **5**, 240.

Mr. Howard G. Hanley: The following data were obtained from a study of 200 consecutive cases of acute *B. coli* pyelitis in women of the child-bearing age (15 to 47). There are 100 non-pregnant and 100 pregnant patients.

A diagnosis of pyelitis is incomplete without ascertaining where the primary pathology or infection lies, since I am sure that the pyelitis is only a dramatic incident in the course of a generalized urinary tract infection.

A full urological investigation was performed in every case—whether it responded to chemotherapy or not. 18% of the non-pregnant and 16% of the pregnant cases were found to have some gross urological abnormality such as calculus, hydronephrosis, tuberculosis or a congenital lesion, e.g. hydro-ureter, ectopic or horseshoe kidney or double pelvis.

32% of the non-pregnant and 37% of the pregnant women gave a history of some previous urinary tract infection, e.g. pyelitis, cystitis or urethritis.

The most important group contained the women with a urethro-trigonitis which usually preceded the onset of the pyelitis. Cysto-urethroscopy showed that 44% of the non-pregnant and 37% of the pregnant women had urethral polypi, inflammatory strictures or lesser pathological conditions which subsequently required diathermy fulguration or urethral dilatation.

Seven cases of "honeymoon pyelitis" were encountered, all of whom had an acute urethro-trigonitis. This type of pyelitis can occur in married or even parous women as well as in newly married patients.

The fact that sexual intercourse or instrumentation in the presence of urethral inflammation can precipitate an attack of pyelitis, is strong presumptive evidence that the pyelitis is an ascending infection from the lower urinary tract.

By combining the cases with gross disease, those with a previous history of urological infection and the urethro-trigonitis group, 69% of the non-pregnant and 54% of the pregnant women had a focus of infection in the genito-urinary system which might easily have precipitated the pyelitis.

The incidence of pyelitis in pregnant and non-pregnant women was almost the same, and I feel that there is nothing special about "pyelitis of pregnancy"; it is merely a pyelitis occurring in a pregnant woman but owing to the physiological dilatation the symptoms are more severe and the treatment is more difficult.

Treatment.—In 1939 hexamine mandelate therapy was substituted with benefit for the usual alkaline diuretic mixtures. In 1942 sulphathiazole was adopted routinely and made a dramatic reduction in the severity of the disease. Alkalis are useful to protect the patient from the effects of fever and to combat acidosis.

Following the increased use of chemotherapy by general practitioners since 1942, the number of cases of acute pyelitis admitted to the hospital has dropped by over two-thirds, while really severe cases are now rare. Twelve of the pyelitis of pregnancy patients required pelvic lavage, ten of them prior to the chemotherapy period.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[January 26, 1945]

Medicine in Jungle Warfare

By Brigadier N. HAMILTON FAIRLEY, C.B.E., F.R.S.

Director of Medicine, A.M.F.

In jungle warfare far more casualties arise from disease than from enemy action. During the earlier New Guinea campaigns casualties from sickness were five to thirty times as common as battle casualties, and malaria and dysentery proved a more serious menace than the Japanese. For this reason it became necessary to instruct every soldier how to avoid disease in the jungle, especially as most of these diseases were avoidable. Training in tropical hygiene now constitutes an integral part of training for jungle warfare.

Owing to the numerous diseases transmitted by biting insects, the clothing of the soldier in the jungle is of major importance. Shorts are dangerous for though they are cool to wear, they increase the surface area of exposure to trauma and insect bites, increase the incidence of tropical ulcers, septic sores, dengue, filariasis and malaria and prevent the effective application of anti-mite fluid for the prevention of scrub typhus. Trousers, gaiters and long-sleeved shirts are essential in jungle warfare.

An analysis of the types of sickness casualties during six months' campaign in the Huon Peninsula and the Markham-Ramu Valley are shown below:

Malaria	60.5%
Dengue	17.5%
Dysentery and diarrhoea	6.5%
Scrub typhus	2.5%
Skin and other diseases	13.0%

The ratio of sickness to battle casualties was approximately 16:1.

BACILLARY DYSENTERY

Bacillary dysentery had been the most frequently encountered disease transmitted by infected food and polluted water. Human carriers and flies are important factors in the dissemination of this disease. In the Middle East, fly transmission was the common mode of spread; in the South-West Pacific and Netherlands East Indies infection by polluted water is common; this is due to the habit of the natives in defaecating directly into streams and rivers.

Early in 1941 in the Middle East 30 lb. of sulphaguanidine were sent to Colonel Buttle by Professor Marshall of Baltimore. Colonel J. S. K. Boyd and the writer investigated its therapeutic value, limiting observations in the first instance to severe cases of bacillary dysentery where the organism had been isolated. Shiga infection was specially studied as this was the only form of dysentery liable to be fatal. Our findings which were reported in 1942 proved conclusively that sulphaguanidine was a specific cure for Shiga dysentery as well as for the milder dysenteries of Flexner-Boyd type. Owing to the necessity for identification of the organism in the early cases investigated, it was generally not feasible to give the drug until the third or fourth day of the disease. As anticipated, later experience showed that the administration of sulphaguanidine in adequate dosage within a few hours of onset, resulted in a dramatic cessation of the diarrhoea, the early production of normal stools and rapid cure. In such cases the disease is practically aborted since multiplication of dysentery bacilli is terminated before the colonic mucosa is seriously damaged. Convalescence is correspondingly shortened and many cases are cured without needing to be admitted to hospital. Several results have followed the widespread use of sulphaguanidine in adequate dosage in the Field and hospitals in New Guinea: (1) The admission rate to hospital has been markedly lowered. (2) The disease appears to be changing its character or disappearing; this is indicated by the fact that it is now only possible to isolate dysentery bacilli in approximately 10% of diarrhoeal cases admitted to hospital. (3) The mortality rate in the last 10,000 cases had been 1:5,000.

More dramatic evidence of its value from a military viewpoint was obtained during fighting over the Owen Stanley Ranges on the Kokoda trail in 1942, when severe dysentery broke out in Australian troops. Japanese troops were at this time dying from dysentery and both forces had, of necessity, polluted the area in the immediate vicinity of the narrow jungle trail, along which successive advances and retreats were

being made. As the epidemic increased in severity, grave concern was felt regarding the dysentery casualties in the Australian Forces. At this juncture all the available reserve of sulphaguanidine in Australia was rushed by air to Moresby and transported to the forward area, where all troops with diarrhoea were immediately treated. At each Regimental Aid Post (R.A.P.) established along the trail at intervals of a few miles, sulphaguanidine in doses of 4 grammes (1 drachm) was administered to troops with diarrhoea or dysenteric symptoms. The result was remarkable. Within ten days the epidemic was completely controlled, and subsequently the incidence was reduced to the number of sporadic cases preceding the epidemic. Here sulphaguanidine acted by breaking the vicious circle. It reduced the number of stools, rapidly controlled the diarrhoea, and so limited the area polluted; by inhibiting the multiplication of dysentery bacilli in the stools, *B. dysenteriae* was either eliminated or so greatly reduced in number that infectivity was minimal. It was the considered opinion of many officers in the A.A.M.C. that sulphaguanidine saved Moresby.

It is not proposed here to assess the relative merits of the different sulphonamides in the treatment of bacillary dysentery. Sulphaguanidine has to be given in large dosage and is expensive. On the other hand, it has proved to be absolutely safe for Field use. In the thousands of cases of dysentery for which it has been used in New Guinea, no instance of anuria has been reported, even though patients have been dehydrated in the initial stages of treatment, nor has agranulocytosis or exfoliative dermatitis been encountered. Rarely headache, nausea, mild erythematous or maculopapular rashes with or without slight fever have occurred, but toxic manifestations of any real severity have been absent. When it is remembered that the mortality in New Guinea from bacillary dysentery treated with sulphaguanidine is only 1:5,000, one has to be very sure not to add to it by substituting a more toxic drug. The disadvantages of sulphapyridine, sulphathiazole and sulphadiazine are their toxicity and especially their tendency to produce anuria in dehydrated patients.

SCRUB TYPHUS

Scrub typhus is transmitted by the bite of larval trombiculid mites harbouring *Rickettsia tsutsugamushi*. Field mice and rats are known to be natural hosts.

Mortality.—This is the only disease which is killing troops with regularity in the S.W.P.A., the overall case mortality rate being about 8%. The mortality rate is found to vary considerably in different areas from 0 to 30%, and this appears to be due to variation in virulence in the strain of *Rickettsia* rather than to variable dosage.

Prevention.—(1) *Anti-mite fluid*: In the Australian Army individual treatment of clothing is carried out with dibutyl phthalate which kills but does not repel mites. Dibutyl phthalate is also used in preference to dimethyl phthalate not because it is a more effective mite larvicide, but because in New Guinea McCulloch found its larvicidal effect persisted longer in clothing after immersion in water and after washing. When wearing treated clothing (socks, trousers and shirt) it is possible to lie down in country swarming with mites without getting a single bite. Complete protection against scrub-itch as well as against scrub typhus is thereby attained. When clothing is removed at night it is essential that the blankets be treated if mite bites are to be avoided. Mites causing scrub-itch are not necessarily concerned with mite typhus.

(2) *Delimitation of infective areas*: Scrub typhus is restricted to small areas of high infectivity often widely separated from one another; generally they occur in association with jungle-fringed streams. For this reason it is important to get immediate notification of typhus cases and for suspected areas to be delimited and put out of bounds to troops immediately.

Treatment.—No specific treatment is known. The sulphonamides and penicillin are only useful for secondary bacterial complications.

DENGUE

In the tropics and sub-tropics the rapid spread of dengue and the fact that it may prostrate as much as 60% of a force make it formidable from a military viewpoint. Though the disease is non-fatal, it may incapacitate the victims for three weeks or longer.

The common mosquito vector was first experimentally demonstrated in Australia by Cleland, Bradley and MacDonald (1916, 1918) to be *Aedes aegypti*. Later, in the Philippines, Simmons (1931) showed that *Aedes albopictus* transmitted the disease. *Aedes scutellaris* was recently proved to be a vector in New Guinea (1944) by Army investigators working under Lt.-Col. MacKerris, A.A.M.C. The density of this mosquito in and around camp sites was reported by Berril and other entomologists to be approximately directly proportioned to the number of cases of dengue occurring in that particular area. In breeding, *Aedes scutellaris* prefers clean rain-water with or without the addition of a few dead leaves. Larvæ breed in rusted tins, old coconut shells, the

tops of oil and petrol drums, and in the axils of the limbs of mango trees. The adults were found to enter tents and huts at approximately 7 to 8 a.m. and 4 to 7 p.m. On overcast days, however, mosquitoes of this species entered and were liable to bite all day long. During the day they appear to rest in cool, damp, well-shaded situations under growing shrubs and bushes, well protected from the rain. Their flight range appears limited to approximately 200 yards.

Experimental transmission to man.—Mosquitoes of four different species were fed in the Finschhafen area, New Guinea, on dengue patients during the first two days of fever, and subsequently flown to Sydney where dengue does not occur. The mosquitoes were kept at the Zoological Department, University of Sydney, and the volunteers at 113th Australian General Hospital under Captain P. G. Dowling. Three volunteers receiving 32 to 82 bites from *Aedes scutellaris* over a period of from nine to fourteen days, each developed clinical dengue characterized by a saddle-back type of temperature and rash. On the other hand, three other volunteers bitten by *Armigeres breinli*, three bitten by *Armigeres milneensis* and two bitten by *Aedes aenigmatus* failed to develop the disease. The infection was also transmitted by subinoculation from the cases bitten by *Aedes scutellaris* to three new volunteers, and from them in turn to four other volunteers. Finally the original volunteers who had developed dengue after being bitten by *Aedes scutellaris*, showed no response on subinoculation of blood containing dengue virus; this demonstrated they had acquired immunity during their original attack.

Prevention.—No drug at present available will affect the course of this disease and no prophylactic vaccine is known. However, in New Guinea during an epidemic it was found that much could be done by: (1) Eradicating breeding places in and around camps; (2) destroying adult mosquitoes by spraying tents and huts especially in the morning (8 to 9 a.m.) and later in the afternoon (4 to 7 p.m.); (3) wearing protective clothing and applying repellent lotion during the day-time; (4) keeping all febrile patients throughout the day and night under mosquito nets. Once a force has been exposed to an epidemic of dengue, sporadic cases may subsequently crop up from time to time, but they do not become numerous unless large numbers of non-immune reinforcements have been introduced in the interim.

MALARIA

When jungle fighting in New Guinea, troops have generally contracted both malignant and benign tertian infections. During active operations they have broken down with the dangerous malignant tertian malaria (*P. falciparum*), and after treatment in hospital have later relapsed with *P. vivax* infections which had not been cured. Throughout the Milne Bay and Buna-Gona campaigns in 1942 malaria casualties far exceeded battle casualties, the hospital admission rate in three to four months almost equalling the total strength of the Forces involved. In these campaigns suppressive treatment consisted for the most part of quinine grains 10 daily. Later, in 1943, there were very heavy malaria casualties in the Ramu and Markham Valley and the Huon Peninsular campaigns, when the suppressive drug regime consisted of 0.1 gramme of atebirin (mepacrine) daily on six days of the week.

So serious were the malaria casualties that in 1943 it was decided by the C-in-C. on the advice of the D.G.M.S. to create a research centre in Northern Queensland to investigate the precise value of all known anti-malarial drugs. A medical Research Unit was formed comprising medical specialists, entomologists, parasitologists and biochemists, and 500 volunteers were soon forthcoming from the Army. The plan was to expose volunteers taking a specified daily dose of a given anti-malaria drug to bites of mosquitoes infected with *P. vivax* or *P. falciparum* parasites. Volunteers took the drug before, during and for twenty-three days after exposure to infection. The latter figure was selected as it constituted the upper limit for the ordinary incubation period for primary malignant tertian and benign tertian malaria.

Only brief reference can be made to the findings in volunteers infected with New Guinea strains of *P. vivax* and *P. falciparum* when taking quinine or atebirin (mepacrine).

QUININE.—**Malignant tertian malaria:** When volunteers, who were taking 10 grains of quinine daily, were exposed to ten infective bites by mosquitoes (*A. punctulatus* var. *typicus*) harbouring sporozoites of *P. falciparum* in their salivary glands, they invariably developed malignant tertian malaria with fever, splenomegaly and parasites in the blood within the usual incubation period. When the dosage of quinine was increased to grains 30 daily the fever was rapidly controlled and generally parasites disappeared in three days.

Benign tertian malaria.—In volunteers exposed to ten bites of anophelines infected with *P. vivax*, grains 5 of quinine daily were found inadequate to suppress overt attacks of benign tertian malaria. When the dosage was increased to grains 10 daily in another group of volunteers suppression was satisfactory in two-thirds of the cases. In view of

being made. As the epidemic increased in severity, grave concern was felt regarding the dysentery casualties in the Australian Forces. At this juncture all the available reserve of sulphaguanidine in Australia was rushed by air to Moresby and transported to the forward area, where all troops with diarrhoea were immediately treated. At each Regimental Aid Post (R.A.P.) established along the trail at intervals of a few miles, sulphaguanidine in doses of 4 grammes (1 drachm) was administered to troops with diarrhoea or dysenteric symptoms. The result was remarkable. Within ten days the epidemic was completely controlled, and subsequently the incidence was reduced to the number of sporadic cases preceding the epidemic. Here sulphaguanidine acted by breaking the vicious circle. It reduced the number of stools, rapidly controlled the diarrhoea, and so limited the area polluted; by inhibiting the multiplication of dysentery bacilli in the stools, *B. dysenteriae* was either eliminated or so greatly reduced in number that infectivity was minimal. It was the considered opinion of many officers in the A.A.M.C. that sulphaguanidine saved Moresby.

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Section of Odontology

President—H. T. ROPER-HALL, M.B., M.D.S.

[January 22, 1945]

The Prosthetic Aspect of the Buccal Inlay Operation [Abstract]

By B. W. FICKLING, F.R.C.S., L.D.S.

(Maxillo-Facial Unit, Hill End Hospital, E.M.S.)

The shape of the mould and its effect upon the site of incision.—To secure a natural contour it is necessary to create, or even to emphasize, the normal groove between the red margin of the lip and the mental prominence (fig. 1, ii). This occurs most readily when the junction between the graft and mucous membrane on the internal aspect of the lip exactly corresponds to this depression on the surface. There is always a tendency for the mucous membrane-graft junction to show some degree of contraction, and this can be encouraged. I call this the "contraction-line" and all my cases show it in a marked degree. It greatly increases the retentive shape of the cavity.

In order that this line shall occur at the correct point it is necessary to plan the incision at operation. In very bad cases of loss of sulcus there is little intra-oral mucous membrane, the contraction line is necessarily high and the result good (fig. 1). When there is a fair length of intra-oral mucous membrane the incision should be made somewhat towards the lip aspect, in order that the contraction line may develop at the correct level (fig. 2).

The moulds are shaped so as to develop the contraction line at the correct level. At operation, the mould must be much larger than will ultimately be required, and all tissue must be placed upon the stretch. So far as possible it is shaped to give a slight groove at the mucous membrane-graft junction. Subsequently this is deepened and emphasized until the facial contour approximates to normal.

Adaptation and fixation of the mould.—When teeth are present the method of fixation usually described is by means of a splint cemented to the teeth and carrying a rod to which the tray is attached by a sleeve and set-screw. This is somewhat bulky; being a one-point attachment it is unstable and very subject to leverage, and a denture cannot readily be applied around it in the later stages of treatment. The tray is placed at right angles to the teeth and at operation it is pressed down upon the mould and removed several times as the shape is adjusted. This presents some difficulty when an excess of gutta-percha is present, and the material is apt to extrude on the lingual aspect and become involved in undercuts.

This fixation has been modified with satisfactory results. The attachment of the tray to the splint is by two 6 BA screws, and therefore the routine threaded plates employed in fracture fixation are suitable. The tray is constructed to fit the alveolus where teeth are missing and so the mould material does not escape on the lingual side. The plate is screwed into position and remains in situ during the construction of the mould. To facilitate the insertion and removal of the mould the plate is attached to the teeth at a slight angle, although the freeing of the lip, which is an essential part of the operation, makes access quite easy (fig. 3). In edentulous cases the difficulties of fixation are much increased. The following method has proved successful, and avoids the need for an intermediate appliance. A denture is constructed to fit the available alveolus with great accuracy and employing every device to increase stability. The teeth are so ground that the direction of the bite is markedly downwards and backwards, and not downwards and forwards as is usually the case. The anterior portion is carried forward at an angle over the area requiring the inlay just as is the metal tray in other cases. The anterior teeth are set up to produce an æsthetic result, being of course anterior to the ridge. The mould material is inserted beneath the anterior extension on the dentine

the complete failure of quinine to suppress malignant tertian malaria and its partial failure to suppress benign tertian infections, it is evident that the heavy malaria casualties in the Milne Bay and Buna-Gona campaigns could not have been prevented by suppressive quinine in a dosage of grains 10 daily even if it had been taken regularly which is very doubtful.

ATEBRIN.—On the other hand, results quite beyond expectation were obtained in volunteers receiving one tablet (0.1 gramme) of atebtrin on six or seven days of the week for four weeks prior to exposure to infection, during the period of exposure and for twenty-three days after the last infective bite. Controls, not taking drugs, who were bitten by the same number of infective mosquitoes from the same batch invariably developed malaria.

(1) *Benign tertian malaria.*—Volunteers exposed to bites of mosquitoes infected with *P. vivax* did not develop attacks of overt malaria when receiving atebtrin with unvarying regularity in the above dosage. But in every case clinical malaria associated with parasites developed later, fever appearing in fourteen to forty-four days, and parasites from nineteen to forty-six days after drug administration ceased.

(2) *Malignant tertian malaria.*—Similarly, volunteers exposed to ten to twenty-one infective bites (*P. falciparum*) failed to develop overt attacks of malaria when following an identical suppressive atebtrin regime. Mild clinical features associated with a slight transient rise in temperature and perhaps some tenderness or enlargement of the liver and spleen were occasionally noted, but in no instance were symptoms sufficiently severe to necessitate bed rest and the volunteers invariably carried on their routine activities. In such cases parasites were never demonstrable though 1 to 2 c.mm. of the blood were examined in thick films. Furthermore, after cessation of drug treatment, overt malaria never developed. Subinoculation of fresh volunteers with 200 c.c. of their blood failed to produce infection, and susceptibility tests invariably showed the original volunteers were capable of developing malaria when they were infected with blood containing malignant tertian parasites.

The continued absence of fever and demonstrable parasites, the failure of subinoculation to transmit malaria and the final demonstration of susceptibility constituted a chain of evidence indicating that malaria infection had been either prevented or cured. Early subinoculation from the seventh to tenth day had, however, revealed parasites in the blood even though they could not be demonstrated microscopically. It is therefore evident that in malignant tertian malaria atebtrin is not acting as a casual prophylactic, but is curative in action, destroying the young asexual parasites as they emerge from the endothelial cells (first tissue stage) early in the disease.

(3) *Mixed infection.*—Reference has been already made to the fact that in jungle warfare most troops become infected with both *P. falciparum* and *P. vivax*. To reproduce field conditions experimentally it was therefore necessary repeatedly to infect troops by exposure to different batches of mosquitoes harbouring *P. vivax* or *P. falciparum* over a period of several months. In addition it was essential to subject them to conditions which favour malaria relapses such as physical fatigue, cold, anoxia, loss of blood, &c. All this was done, but in no instance did overt malaria develop while they were taking atebtrin. But on an average of thirty days following cessation of drug administration every volunteer developed benign tertian malaria. Parasites of *P. falciparum*, however, were never found. These experiments were of profound significance from a military point of view for they proved that, provided troops took atebtrin in adequate daily dosage as laid down in standing routine orders, it was possible for them to go into hyperendemic areas of malaria and fight for indefinite periods in the jungle without malaria casualties. Theoretically there would be no malaria admissions to hospital, no deaths, no carriers and no blackwater fever—always provided the daily dose was continued for three to four weeks after leaving the endemic area. After stopping atebtrin troops infected with latent *P. vivax* would develop overt benign tertian malaria.

FIELD EXPERIENCE

The validity of these conclusions has been strikingly demonstrated during the past fifteen months in the S.W.P.A. Following an increasingly efficient atebtrin discipline the malaria admission rate to hospitals in New Guinea has fallen almost progressively from 740 per 1,000 per annum in December 1943 to the remarkably low level of 26 per 1,000 per annum in November 1944, despite the fact that many of the troops are still located in hyperendemic areas of the disease. A number of factors besides atebtrin have contributed to this result. These include less fighting and static conditions which have enabled more effective control of larval breeding and destruction of adult mosquitoes, &c., and therefore less fresh malarial infections. Many of these troops, however, have chronic benign tertian malaria and the infrequency of malaria relapses shows conclusively that atebtrin is the dominant factor in maintaining the hospital admission rate at so low a figure.

(fig. 4). Below the teeth a twin-screw fixation is employed to carry an extra-oral bar. This is connected by light elastic tension to a trough fitting the surface of the neck beneath the mandible which is retained in position by elastoplast strapping. After six to ten days the extra-oral fixation is discarded and retention must rely on the shape of the mould and the efficiency of the bite.

The intermediate appliance.—There is a great tendency for rapid contraction to take place in buccal inlay cavities for a considerable time after operation. This period is often underestimated and is probably longer in gunshot wounds with external scarring than in cases of developmental origin. To improve appearance and function a prosthesis carrying teeth and improving contour should be inserted at as early a date as possible. It is practicable to have teeth on the appliance from the beginning, as in edentulous cases, and in these there is no intermediate stage. In others the tray is discarded and a denture inserted in its place. To avoid the hiatus of several days which would occur should the splint be removed and impressions taken for construction of a denture fitting the teeth, I prefer to make a denture fitting round the splint and sometimes lock this in position by inserting a screw through the denture into the splint. By this means positive pressure can be maintained for a lengthy period and the patient has a stable appliance during the early stages of the process of adaptation to dentures. The mould is still made unduly large and is gradually reduced in size as the tissues contract and the final contour is visualized.

The final appliance.—The alveolar portion of the final appliance is constructed to a good impression, and the bite requires careful adjustment. The portion filling the inlay cavity is shaped in wax and in general follows the design of the intermediate moulds. The groove for the contraction line becomes less marked as the over-correction in the mental region is reduced. Contour is often much improved by cutting away the central projecting portion to accommodate the mental pad of fat (fig. 1).

[See also Fickling, B. W., *Proc. R. Soc. Med.*, 1943, 37, 7.]

Mr. P. Rae Shepherd said that one of the main features which the paper stressed was the necessity of making a really large inlay cavity; with this he was in complete agreement. The common mistake of the beginner was to make the cavity far too small.

Recent Advances in the Treatment of Jaw Injuries [Abstract]

By ALEXANDER B. MACGREGOR, M.A., M.D., B.Chir., M. and L.D.S. R.C.S.,

S/Ldr. R.A.F.V.R.

THE whole subject was briefly reviewed, and progress since the beginning of the present war outlined. It was stressed that, with few exceptions, advances had been mainly in technique rather than in the application of new principles. Cast metal cap splints still remained the basic anchorage of choice, where teeth were present, and facilities for their manufacture available. The essential principles in their manufacture and use had been well dealt with by Fry, Shepherd, McLeod and Parfitt (1942). Interdental and arch wiring were still of great value particularly where conditions militated against the use of cap splints. Acrylic splints, though simple to manufacture, were bulky in the mouth, particularly where locks or attachments for bars had to be incorporated in them, and they had not been found in consequence to fill a very useful role.

For maxillary fractures the speaker pointed out that the plaster headcap applied over stockinet continued to be used as a fixed point for immobilization of maxillary fragments through the intermedia of bars and wires. This headcap was only a relatively fixed point owing to scalp movement over the skull, and, hence, was by no means perfect. Suggested methods of obtaining rigid fixation, such as transfixion of the bone of the supra-orbital ridges, had not found much favour, and the plaster headcap, though imperfect, remained the standard base for methods of fixation of the maxilla. Numerous photographs were shown to illustrate the varying techniques of supporting the maxilla, ranging from the complex apparatus shown in fig. 1 by which precision adjustment in all planes could be obtained, to the simple method previously described by MacGregor (1944) in which wires attached to horns projecting from the headcap are passed through the cheeks, to be attached to a mandibular arch-wire, fixed by rubber bands to a maxillary arch-wire.

The difficulties of reposition of the maxilla, particularly in bringing it forward or getting it up at the back after displacement, even after mobilizing the fragment, or fragments, with lion or other forceps were stressed. Photographs were shown of patients

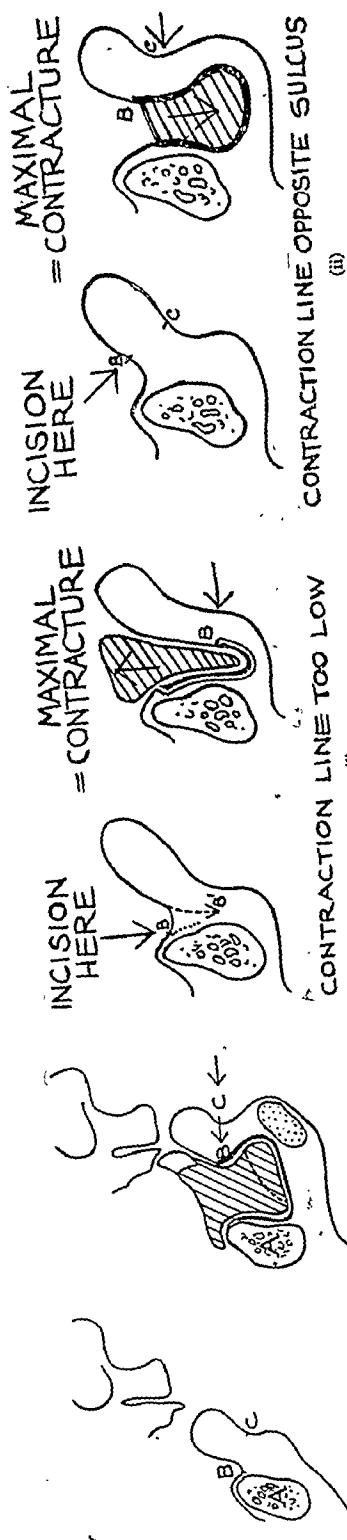


FIG. 2.—(i) Less severe loss of buccal sulcus. (ii) The normal point of incision makes the mucous membrane-graft junction too low. (iii) Incision made toward the free margin of the lip so that the mucous membrane-graft junction occurs at a level giving the best facial contour.

FIG. 1.—(i) Profile drawings of the face showing inferior rotation and lack of buccal sulcus, corrected by the insertion of a mould into a buccal inlay. A, the normal point of incision; B, the normal point of incision, becomes the mucous membrane-graft junction, which corresponds in level with the intra-labial depression C. In the final stage of treatment the portion of mould below the dotted line may be cut away in the mid-line to accommodate the mental pad of fat.

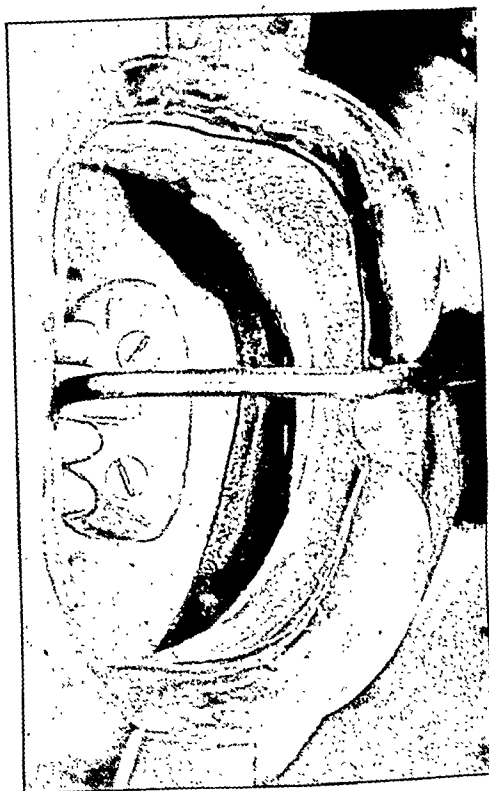


FIG. 3.—Tray for retention of buccal inlay mould, cast to fit the alveolus and attached to the splint by a Thiersch graft. The cavity is lined with a Thiersch graft and the contraction line developed at the mucous membrane-graft junction is apparent.

FIG. 4.—Denture, with extra-oral attachments, constructed in advance to retain the mould of black gutta-percha shaped at operation. The contraction line can be seen.



FIG. 2.—Apparatus employed for pin fixation with 3 mm. stainless steel pins in a patient with bilateral fractures of the mandible with gross downward displacement of the middle fragment.



FIG. 3.—X-ray of mandible of patient shown in fig. 2 to show tilting and downward displacement of the middle fragment before treatment.



FIG. 5.—Electrolytic action causing ulceration of the area surrounding the pin and disintegration of the pin itself.



FIG. 4.—X-ray of mandible of same patient to show retention of the middle fragment in correct alignment by the 3 mm. pin apparatus alone without adjuvant methods.



FIG. 6.—Ulceration of the mucous membrane opposite a fixation block on a cap splint, in which a stainless steel nut has been cast into the block. The nut itself has partially disintegrated.

(Photographs shown in figs. 5 and 6 were kindly taken by Mr. Paul Toller.)

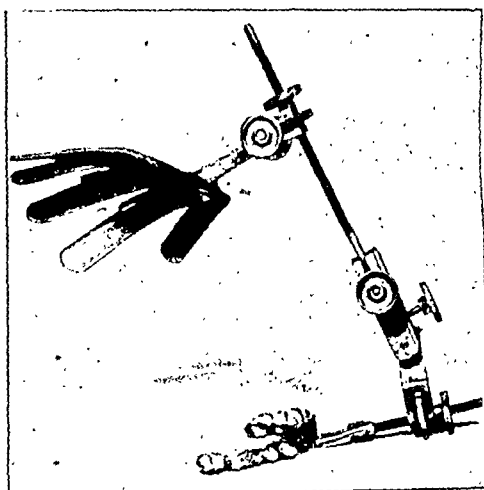
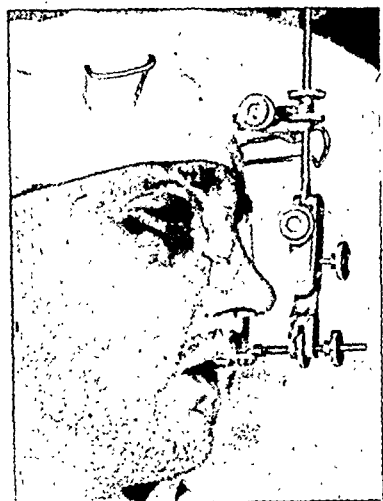


FIG. 1.—Machine for incorporation in a plaster headcap, where accurate replacement or slow traction is required. The apparatus is attached to the upper cap splint by bolts, and screw traction can be applied in any direction.

who had had slow screw traction, or traction applied by weights over pulleys, over prolonged periods after operative mobilization, in whom the maxilla, though in good functional position, had not been fully restored to its old anatomical level.

No marked advances had occurred in the treatment of fractures of the malar-zygomatic complex, though pins or screws were now more frequently employed to hold the main fragment in position in difficult cases.

It was made clear that in fractures of the mandible it was not intended to deal with the simpler types of fracture, which were still treated by the routine methods, but rather to concentrate on certain aspects of treatment in which advances had been made, or further knowledge gained. Experience had shown that many fractures of one or both condyles of the mandible, where the bite was unaltered, could be treated without any fixation. If the occlusion was altered, fixation was necessary. Late cases with a gross alteration in occlusion interfering with function were best treated by condylectomy, since efforts to fix the condyle to the neck of the mandible by wiring after refracture, or other procedures, had proved unsatisfactory. Condylectomy gave an excellent functional result.

Circumferential wiring of a metal trough or splint lined with gutta-percha to the bone of the mandible was not employed so frequently since the advent of the pin fixation method. It was still often of value, however, with children in whom the presence of unerupted permanent teeth deep in the mandible, made the use of pins dangerous.

Pin fixation of fragments of the mandible in edentulous patients, or in patients in whom it was necessary to control the difficult edentulous posterior fragment, had proved to be a great advance in treatment.

The stages in evolution of the crossed pin technique were traced and illustrated with photographs. With this technique in which crossing pins were drilled through the skin into the mandible, and then attached by means of clamps and bars to another set of such pins or to a cap splint on the teeth, treatment of difficult cases had been greatly facilitated. At the Hill End unit many modifications in the original apparatus had been made, and a light and adaptable form of it for use with 1.5 mm. diameter pins had been previously described (Mowlem *et al.*, 1941). This was lighter than the Clouston-Walker (1943) splint though the latter had proved very adaptable. Later experience had shown that these 1.5 mm. pins were not sufficiently strong to withstand the strain occasionally placed upon them, particularly for example where there were bilateral fractures of the mandible with downward hinging of the anterior fragment. A new and stronger apparatus was in consequence now being used incorporating 3 mm. diameter pins with shouldered points. With this apparatus alteration in the position of the fragments after operative fixation, due to bowing of the pins, no longer occurred, and it was now possible to hold the middle fragment in position in patients with bilateral fractures of the mandible without recourse to adjuvant methods of retention (see figs. 2, 3, 4).



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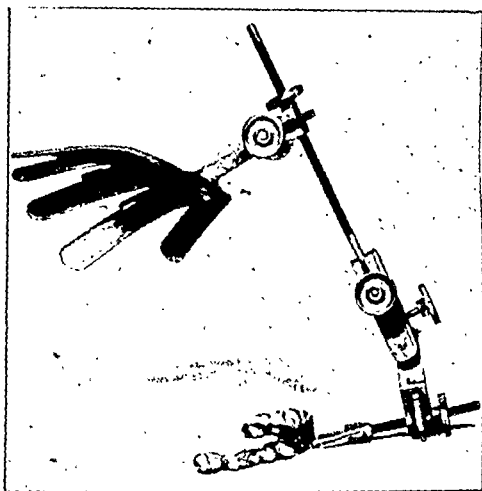
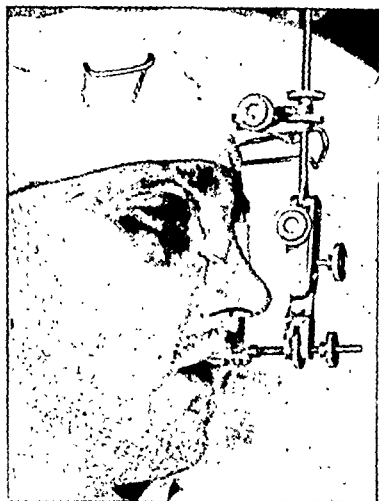


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Section of Physical Medicine

President—L. DANYERS BAILEY, C.B.

[January 10, 1945]

The Management of Rheumatoid Arthritis [*Abridged*]

By FRANCIS BACH, D.M.

THE four main clinical and pathological forms of rheumatism are rheumatic fever, the rheumatoid type of arthritis, the osteo-arthritis type and non-articular rheumatism or fibrositis.

Although these forms of rheumatism are differentiated it is the sick man and not the disease process that we are called upon to treat. People react in different ways to similar extraneous stimuli. In the causation of disease there are both extrinsic and intrinsic aetiological factors. The resistance of the individual is inversely proportionate to individual predisposition. Predisposition is not an individual entity but a product of structural and functional components of the individual, both constitutional and environmental in character. Constitutional biological inferiority, poverty, malnutrition and occupation are some of these components. They determine whether or not a disease may result from the action of seemingly insignificant injurious agents. They are responsible for the individual difference in the clinical picture and course of the disease. The rheumatoid type of arthritis, although not the most common rheumatic condition seen in medical practice, produces a greater amount of crippling and more need for early institutional treatment than any other form. It is essentially a disease affecting the young adult and is more common in women than in men. The clinical picture may manifest itself as an acute febrile polyarthritis. Usually the onset is insidious, and the disease runs a course of many years of remission and exacerbation. The common constitutional type is the overworked, tired, worrying, tense, underweight, slender individual of a poor posture and with cold clammy hands and feet. Worry, emotional strain, overwork, sudden shock and malnutrition stand out in the carefully taken clinical history. Commonly the patient is a young woman who complains of fatigue, loss of appetite, backache and vague pains, rapid heart beat, loss of weight and, later, of transient stiffness and puffiness of one large joint such as the wrist, knee or ankle or the proximal interphalangeal joints of the hand. Generally the correct diagnosis is not made at this stage and symptomatic treatment only is given. The local signs respond to local treatment but a few months later the patient complains on waking in the morning of aching stiffness with restriction of joint movement in one or two of her fingers or of pain, muscle spasm and limitation of movement in a wrist or ankle. There is pain on movement of the joint and acute tenderness on lateral pressure on the slightly swollen puffy interphalangeal joints. Later muscle wasting, joint deformity and skin atrophy may appear.

Single screws were now being tried in place of the crossing pins in selected cases. Results were promising, but it was too early to give any final pronouncement on their value.

Mowlem's (1944a) method of chip bone grafting had proved one of the real advances in this type of work, but had necessitated a revision of previous views on fixation while the graft was taking. The old solid type of cortical graft mortised or wired into place provided its own support, but with the use of cancellous chips, fixation of the fragments to be bridged by some apparatus was necessary. Pin fixation had proved of great value in, this connexion.

Electrolytic action causing disintegration of metals was of more importance than generally realized, and it was pointed out that considerable care had to be taken to prevent its occurrence. MacGregor and Fickling (1943) had first drawn attention to the ill-effects that could accrue from electrolytic action causing disintegration of pins employed in the pin-fixation technique. It had been found that not only plated steel pins, but stainless steel pins, became corroded when they were connected via metal clamps and bars to a splint in the mouth. This was due to metals far apart in the electromotive series being connected on the one hand by conductor metals, and on the other by the tissue fluid, which formed the electrolyte. Photographs were shown, e.g. fig. 5, of disintegrated pins and the ulcerated areas in patients caused by this process. An insulator was now always included in the metal connexions in order to break the circuit. Photographs were also shown of patients in whom stainless steel nuts, cast into the locking plates of the cap splints, had disintegrated, with ulceration of the neighbouring mucous membrane, presumably due to the same process (fig. 6).

Penicillin has proved of very great value in the treatment of jaw injuries. Many patients had undoubtedly retained bony fragments which later united that would otherwise have been lost, and the value of penicillin in the treatment of osteomyelitis of the mandible had been described by Mowlem (1944b). Recent work by MacGregor and Long (1944) had shown that penicillin pastilles appeared to be of considerable value in the treatment and prophylaxis of jaw injuries compound into the mouth.

The speaker concluded by expressing his thanks to Air Marshal Sir Harold Whittingham, D.G.M.S., R.A.F., Mr. Rainsford Mowlem, and to his colleagues at the Plastic and Jaw Centre of Hill End E.M.S. Hospital for their co-operation and help.

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Mr. P. Rae Shepherd said that although at East Grinstead they used cap splints fairly extensively for the immobilization of fractures, this was not because they thought that wires had no use. In fact they did use wires on the simpler cases which they expected to unite in a short time. But the fewer the natural teeth present and the longer the case was going to be under treatment, the greater the indication for cast silver cap splints.

In fractures of the maxilla, S/Ldr. MacGregor lamented the lack of a secure base to which the mobile upper jaw could be fixed. But surely such a base was there already, namely the mandible. If a plaster headcap was applied, and the mandible fixed to it by means of rods and universal joints, the mandible then provided a very stable base to which the maxilla could be fixed. It was true that neither the mandible nor the plaster headcap was individually stable, but when they were fixed securely together the one immobilized the other very effectively.

When using Roger Anderson pins it was desirable to fix the upper and lower teeth together in normal occlusion to relieve the strain on the pin apparatus. They had found that the original pin appliance with 2 mm. pins was not rigid enough and had substituted 3 mm. shouldered pins with an appropriate increase in the thickness of the connecting bars. This stiffer apparatus had given superior results and encouraged by these they were shortly going to try an even stronger appliance.

They had also been troubled with electrolytic action due to the use of dissimilar metals. When using brass screws and connecting bars in the mouth they coated them initially with either shellac or wax. When this wore off in the course of a week or so, they found no further trouble with electrolysis.

They also had had electrolytic ulcers and bone necrosis around pins when an extension from the cap splints was used; this had been overcome completely by the insertion of an electrical insulator between the pins and the splint.

Mr. Shepherd agreed with S/Ldr. MacGregor that the one fundamental change in surgery which has been made since the war began was the use of medullary bone chips for grafting instead of the solid block of bone. Mr. Rainsford Mowlem had placed them all in his debt for this technique and was to be congratulated upon such an outstanding advance.

Section of Physical Medicine

President—L. DANYERS BAILEY, C.B.

[January 10, 1945]

The Management of Rheumatoid Arthritis [*Abridged*]

By FRANCIS BACH, D.M.

THE four main clinical and pathological forms of rheumatism are rheumatic fever, the rheumatoid type of arthritis, the osteo-arthritic type and non-articular rheumatism or fibrositis.

Although these forms of rheumatism are differentiated it is the sick man and not the disease process that we are called upon to treat. People react in different ways to similar extraneous stimuli. In the causation of disease there are both extrinsic and intrinsic ætiological factors. The resistance of the individual is inversely proportionate to individual predisposition. Predisposition is not an individual entity but a product of structural and functional components of the individual, both constitutional and environmental in character. Constitutional biological inferiority, poverty, malnutrition and occupation are some of these components. They determine whether or not a disease may result from the action of seemingly insignificant injurious agents. They are responsible for the individual difference in the clinical picture and course of the disease. The rheumatoid type of arthritis, although not the most common rheumatic condition seen in medical practice, produces a greater amount of crippling and more need for early institutional treatment than any other form. It is essentially a disease affecting the young adult and is more common in women than in men. The clinical picture may manifest itself as an acute febrile polyarthritis. Usually the onset is insidious, and the disease runs a course of many years of remission and exacerbation. The common constitutional type is the overworked, tired, worrying, tense, underweight, slender individual of a poor posture and with cold clammy hands and feet. Worry, emotional strain, overwork, sudden shock and malnutrition stand out in the carefully taken clinical history. Commonly the patient is a young woman who complains of fatigue, loss of appetite, backache and vague pains, rapid heart beat, loss of weight and, later, of transient stiffness and puffiness of one large joint such as the wrist, knee or ankle or the proximal interphalangeal joints of the hand. Generally the correct diagnosis is not made at this stage and symptomatic treatment only is given. The local signs respond to local treatment but a few months later the patient complains on waking in the morning of aching stiffness with restriction of joint movement in one or two of her fingers or of pain, muscle spasm and limitation of movement in a wrist or ankle. There is pain on movement of the joint and acute tenderness on lateral pressure on the slightly swollen puffy interphalangeal joints. Later muscle wasting, joint deformity and skin atrophy may appear.

To treat the disease it is necessary to understand something of its natural history. A small number of people gradually become crippled in spite of every medical care. In many the disease becomes arrested with little crippling even if inadequate or no treatment is given. In the large majority early and adequate treatment is essential if the progress of the disease is to be arrested and gross deformity prevented.

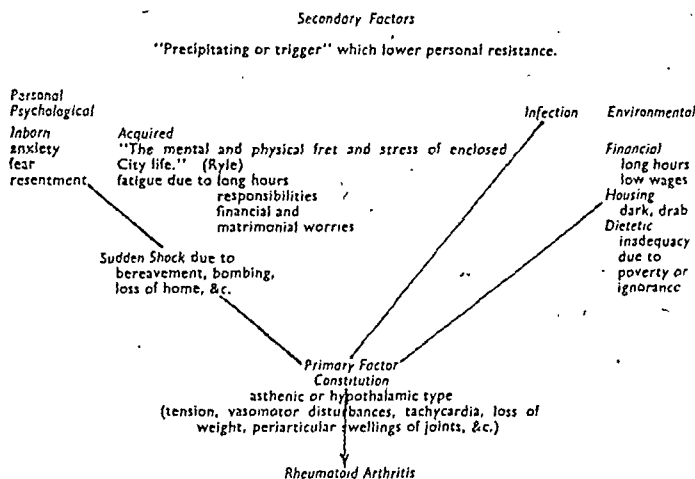


CHART 1

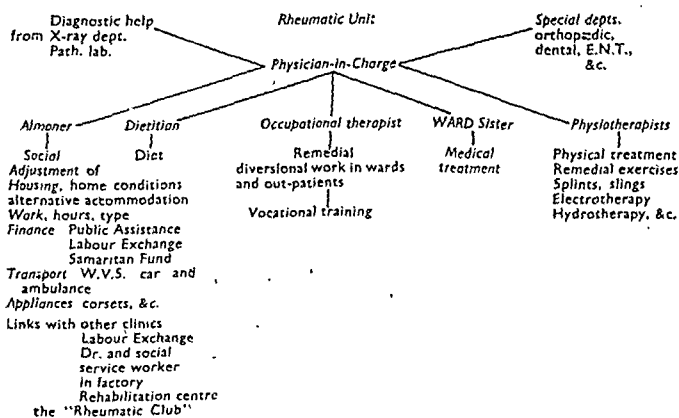


CHART 2

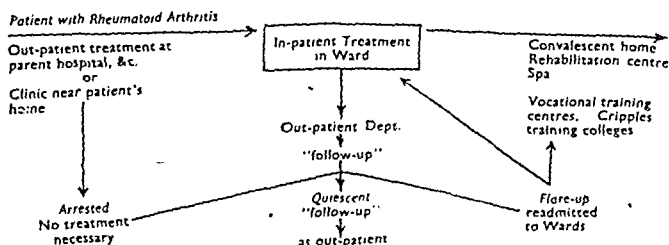


CHART 3

Chart-I shows the primary constitutional factor and the secondary or precipitating factors which are known to produce the clinical picture of rheumatoid arthritis. It will be seen that at this stage environmental and psychological factors are of much greater importance than infection as the secondary factors which precipitate or act as the trigger in the causation of this disease.

The detailed clinical pictures were described of 13 consecutive patients attending at the present time under my care as out-patients at the British Red Cross Clinic. Although there are great differences in their homes and occupations considerable and prolonged worry was a permanent factor in their domestic situations prior to the onset of the arthritis. The trigger factor was most frequently a psychological one. The flare up of the condition that I have noticed while they were under treatment in every case had been preceded or precipitated by a psychological disturbance. The bombing of London played an important part. These few cases were taken from a larger series which we are investigating at the present time.

The second chart is a graphic presentation of the Rheumatic Unit at St. Stephen's Hospital and shows the work of the various members of the team.

The third chart shows the relationship of the parent hospital to other centres to which the patient may have to be sent. It will be seen that the spa, convalescent home and the vocational training colleges play an important role.

In-patient Treatment	
Preliminary investigation—Clinical, Radiological, Pathological	
Treatment	
(i) Rest	psychological, physical
(ii) Drugs	a. to relieve pain, muscle spasm and promote sleep Salicylates, amidopyrine, prostigmine, amytal, &c. b. to treat anaemia and hypochlorhydria Iron, hydrochloric acid dil, liver extract c. to stimulate "reticulo-endothelial system" Gold preparations (Myocrisin, Solganol, &c.) Bismuth preparations
(iii) Endocrine preparations	Cestroform, testosterone propionate, thyroid, suprarenal, insulin
(iv) Vitamin preparations	Nicotinic acid, Benerva Ascorbic acid, Radiostol, Multivite
(v) Diet	High calorie, salt free, small bulk, appetising to increase calorie value and correct vitamin deficiency
(vi) Physical treatment to prevent or correct deformity	Relaxation and breathing exercises (individual or group) slings, springs, pulleys Infra-red, ionization, short wave, U.V.L., mud, pool, &c. Corsets, foot supports
(vii) Orthopædic measures	Splinting with plasters to correct or prevent knee, wrist deformity, &c. Joint aspiration, lavage, capsulectomy, &c.
(viii) Treatment of possible foci of infection	Teeth, sinuses, gall-bladder, pelvic organs, &c.
(ix) Special measures	Blood transfusion, "therapeutic jaundice", splenectomy, sympathectomy
(x) Occupational therapy	Remedial specific, non-specific, diversional
(xi) Advice on course of disease, how to modify it, where to get treatment, "follow-up", "Rheumatic Club", &c.	

The table (above) summarizes the main features of treatment which I am accustomed to carry out in those patients who are under my care. It will be realized that at one time one section of treatment must take precedence whereas in another patient or on another phase of the disease the treatment may be almost entirely confined to another section.

In brief it is my purpose to point out that the successful treatment of the early and active phases of rheumatoid arthritis is dependent on close co-operation between the patient and the medical staff. The latter may consist of a team as in the Rheumatic Unit or of one man as must often happen in general practice. The aim of treatment is to help the patient to increase his or her resistance by altering some of the constitutional and environmental pictures which cause ill-health and by this means to modify the clinical picture of the disease. Psychological, medical, physical and sociological measures play an important part in this achievement.

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The Management of Osteo-arthritis [*Abridged*]

By A. R. NELIGAN, M.D.

THE choice of the word "management" seems a particularly happy one in connexion with osteo-arthritis for, it will be agreed, what may be called his active treatment, limited as it mostly is to the use of heat, is a good deal less important for the patient than the adjustment of his way of life, in other words his "management". Indeed, failing it, the results of such treatment are certain to fall short of what may fairly be expected. But here there is a difficulty: the patient's active co-operation is essential—he is the key man in what may, with his doctor and the expert in physical medicine, be a team of three. And there is another difficulty, the long intervals between courses of expert treatment. Perhaps these difficulties are two of the reasons for the common air of frustration about the whole subject of osteo-arthritis; and another may be the common view of its pathology: a degenerative condition, the result of wear and tear on ageing tissues. There are ways, however, in which these difficulties may be reduced in the home management of arthritis.

Ætiology and prevention.—There are three cardinal factors in the causation and development of osteo-arthritis; their elimination is the aim of treatment and, if taken in hand early enough, they may even be prevented. They are: (1) Injury to the joint surfaces: invariable as a factor—infinately variable in degree—ranges from gross injury (traumatic osteo-arthritis) to ordinary use in susceptible joints (osteo-arthritis of the elderly). (2) Changes in the physiology of the joint affecting the blood and also, presumably, the lymph, circulation, the synovial membrane and fluid, the cartilage. (3) The reaction of the joint tissues—osteophytes, osteosclerosis, thickening of the synovial membrane.

Prevention of osteo-arthritic changes may be effected: (1) By treating injuries of bones and joints and congenital abnormalities of joints. By the removal of loose bodies from joints. (2) By the correction of abnormal strains due often to postural and foot defects. (3) In industry, by reduction of strain and over-use and by improving the environment. (4) By the regulation of exercise and rest in the elderly especially if they are of the osteo-arthritic body type, have Heberden's nodes or belong to arthritic families. (5) By the treatment of obesity. (6) In the thorough treatment of other forms of chronic arthritis especially that of the menopausal type.

It is possible that if more attention were paid to the early joint pains of the elderly, or the injured, the diagnosis of oncoming osteo-arthritis might be more often made before radiographic changes showed that deterioration was well under way.

Indications for management.—The chief indications in the management of an established case of osteo-arthritis are: (1) To secure the co-operation of the patient. (2) To ensure the best possible environment for him. (3) To remove ætiological factors or, at least, lessen their effects. (4) To maintain function. (5) To relieve pain and improve the condition of the joint.

(1) *Explanation.*—The patient's co-operation in his home care is essential and will be, more often than not, obtained by a careful explanation of what is aimed at. He may be told that he is in good health and that his joint trouble is not really an arthritis but the result of wear and tear; therefore the obvious thing to do is to "spare" his hip just as one spares a horse a bit "gone in the forelegs" or a car with worn transmission. Apart from this there are exercises and some simple treatment—in fact a regular programme to be followed without, however, becoming an invalid in any sense. Once learned it will become part of his life and he will need only occasional medical supervision. If he will co-operate, the wearing of his joint may be stopped; it will at any rate be slowed down, pain relieved and leg made stronger. Cure is not possible: on the other hand only one or two joints are likely to be affected and there is no fear for his health or of general crippling. He need not be cast down by what he has seen in his X-ray film.

With regard to this explanation, which incidentally represents my "osteo-arthritis credo", I would add that: (a) The common fear of arthritis would be justification for substituting the term "arthrose" (osteo-arthrose)—which would not carry such serious implications to the patient.

(b) Reassurance about crippling is specially important at spas where many advanced cases of rheumatoid disease may be seen. It can be emphatic in traumatic cases.

(c) The X-ray picture of gross changes is an alarming one to the intelligent layman: for he does not readily believe that they may be compatible with fair function.

(2) *Environment*.—Opportunities for choice or change of external environment will be rare for some time to come but working conditions and the nature of the job should be studied and discussed in each individual case as they may have a most important bearing on arthritis.

The personal environment includes attention to general hygiene, and advice on rest and activity.

(3) *Sparing the joints*, in other words dealing with ætiological factors, is the most important part of management. They should certainly be corrected as far as possible whether they be mechanical, metabolic or endocrinal. Menopausal arthritis is a good case in point for it reacts well to treatment but generally goes on to osteo-arthritic changes if neglected. Most of these patients are, however, in good health and have never apparently abused their joints: then we fall back on some such predisposing factor as inherited deficiency of cartilage. However, whatever the cause, the aim is the same, to "spare" the affected joint. There are three chief ways of doing so, by rest, by modified activity, and in the case of the weight-bearing joints, those most often affected, by weight reduction.

Rest periods are the single essential part of management in osteo-arthritis. A good night's sleep is of course the most important one and, second to it, comes an hour lying down after the midday meal or, if this be not possible, after the day's work. In many cases both periods are needed. An hour a day means fifteen days off the damaged joints in the year and also relief to spasm and wasted muscles, less general fatigue at nightfall and better sleep. Regular holidays, the week-end and a mid-week half-day give opportunities for rest as well as recreation.

Rest periods in industry are now usual and they do good both in prevention and relief, especially in heavy repetitive work.

Activity.—Most osteo-arthritics are cheery, energetic folk, used to working hard and playing hard, so it is wise on general grounds to allow them as much activity as may be judged prudent. They will then be less restive under "management". Moreover, there is the ever-present question of their muscles. "Little and often" is not a bad slogan.

Regulation of activity is not easy in the constantly varying rheumatic condition. Patients often ask about it. It is largely a matter of trial and error. There are, however, two helpful rules, namely, that if any resulting discomfort lasts an hour or disturbs sleep, the activity will have been too great or is unsuitable, and, secondly, that there should be no increase in, but rather less, pain and stiffness next day during similar activity.

In industry there are many obvious ways of relieving workers with arthritis from strain and over-use of their joints and of fitting the job to the man.

As to exercise, each patient offers different problems. It is safe to say, however, that walking (wearing rubber-soled shoes and on turf when possible), bicycling, and swimming in warm water, are the most generally suitable forms, in short spells with occasional rests. Boating, canoeing and bowls are also suitable. Golf can be adjusted to a nicety by holes, and turf lessens jar.

Lastly weight reduction. The diet of the elderly should suit digestion and be well balanced. I think that is about all there is to say about the osteo-arthritic unless he is overweight, as he, or rather she, very often is. Then drastic reduction is an excellent way of sparing spine and legs and may give dramatic all-round improvement.

(4) *Maintenance of function*.—"Management" of general activity helps to preserve joint function in damaged joints, but something more is needed, namely, active stretching of the joint and active training of special muscle groups. They receive too little attention; it is unusual to find patients who know how to do them. Here, again, explanation yields dividends coupled with a warning that massage alone will not restore wasted muscles.

(5) *Treatment of the joints* aims at relieving pain and improving the circulation, deficiency in which seems to be the one common factor in chronic rheumatic conditions; and, if arteriosclerosis is by no means regularly found in osteo-arthritic joints, their owners are at an age when it is common. Moreover, Pemberton has produced osteo-arthritic changes in animals by obstruction of the articular arteries. Both indications are usually met by applying heat by expert methods, in short courses, at more or less long intervals. When, after a few weeks or months, the joint has become painful again, need the patient wait until his work or his pocket will allow him to have another? Why, as heat relieves him should he not have it applied at home, often, even daily, between courses? For some years past patients have been advised to use heat frequently and it is becoming clear that those who do, keep better between courses than those who do not. Happily there are many simple, cheap and effective ways of applying heat in the home, but it is most important to give the patient or his family practical demonstrations of how to

use the method best for himself and in his circumstances. Typed instructions should also be given to him and sent to his doctor. There is scope in the contracting field of general practice for a wider use of physical methods of treatment and one doctor could carry on general supervision of a number of patients, especially with trained assistance.

Expert physical treatment gives opportunities for review and, if the patient leaves his surroundings, he gets other advantages, especially that of regulated rest. More hostels for rheumatic cases, with a treatment centre near-by in pleasant surroundings, would be a boon to the tired and aching osteo-arthritis. The mass treatment of rheumatism is a big subject, and we have still to learn what the late effects of six years of war may be. However, there is no need to say more on the matter, in view of the Empire Rheumatism Council's valuable "Plan for National Action".

The drawbacks of expert treatment may, however, from the point of view of many patients, be very real. It is a question too if the simple ways of applying heat mentioned are much less effective than our more complicated methods, except, perhaps, diathermy in the case of the hip and some forms of bath treatment including the therapeutic pool, though, even here, domestic and local swimming baths may be turned to account. Perhaps, however, the right way to treat worn-out joints with heat is with mild degrees but continuously.

Massage and exercises for the associated muscles, as well as general exercise, also improve the joint circulation and so should attention to varicose veins in the case of the lower limbs. However, fibrositis of muscles and joint capsules are the chief indications for massage in osteo-arthritis.

There are many other points in management especially in the treatment of pain; for instance, the actual cautery for superficial joints, especially the knees. Intercurrent attacks of synovitis, following over-use or injury, demand absolute rest, as do some cases of very painful arthritis when first seen, perhaps with weight extension, or a plaster case.

Persistent joint-pain is unusual, and may mean dense osteosclerosis or some complication such as an added infective element; fracture into or near the joint; osteomyelitis; Paget's disease; new growth. The possibility of a mistake in diagnosis (tuberculous or gouty arthritis) should not be forgotten.

Osteo-arthritis with severe pain or disability.—Some patients have so much pain that ordinary methods fail and their general condition begins to suffer. While it is well to make as close a diagnosis as possible of the cause of pain in all cases of osteo-arthritis, it is doubly important here, for successful treatment depends on it and also because some of the methods of relief in use are not to be lightly advised for elderly people. The pain may be due to one of a number of conditions or a combination of them: periarticular fibrositis; synovitis with perhaps adhesions; loose bodies or fringes; extensive erosion; bony sclerosis; strain due to malalignment after fracture; muscle spasm; or referred pains in arm, trunk or leg may have to be sorted out. In yet other patients gross crippling by, for instance, contraction deformities or two stiff hips demands relief.

If treatment by X-rays will relieve some of these patients, it should be considered before more drastic methods. What are the clinical indications for its use and what results may be expected? Does it, for instance, affect the course of the joint changes?

The results of some of the *new operations*: Fixation of the hip; *débridement* of osteo-arthritic joints; excision of the patella. Does metal in the hip-joint such as by nailing or vitallium cup arthroplasty contra-indicate the use of diathermy? A patient seen last year for traumatic osteo-arthritis following nailing for fracture was convinced that she had had very much more pain after a few treatments.

Drugs.—To do without *analgesics*, i.e. aspirin and its combinations, may be a sign of good management, but they may make all the difference to the start and to the end of the day and should surely not be denied on academic grounds. Many patients say they feel better and have less pain while taking *iodine*. Perhaps they are subthyroidic. Only small doses seem necessary in short courses and over long periods.

The best way to "manage" osteo-arthritis is to prevent it. This requires accurate knowledge of its aetiology. As things are, the adjustment of the patient's home life and work remains the basis of "management". How to secure his co-operation and better treatment by physical methods has been suggested. There is scope for the wider use of these in general practice.

Section of Psychiatry

President—A. F. TREDGOLD, M.D.

[December 12, 1944]

The Causation of Mongolism and Its Prognosis [*Abridged*]

By MARKUS ENGLER, M.D.

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It was Langdon Down who in the *London Hospital Reports* in 1866 first introduced the term "Mongolism" when classifying the feeble-minded and imbeciles according to ethnic standards, at the same time he pointed out the possibility of parental tuberculosis, at least in a great number of cases, as being responsible for this amentia.

One of the first to deal with the problem of heredity with regard to the Mongol was the American Charles Hermann. He as well as Brushfield, Fantham, Orel, Professor Nobel and many others noted that two or even more Mongols had been observed in the same family. They also reported that in a great number of their cases other forms of amentia, neuropathic stigmata and intemperance could be proved in the parents or their families. In a recent publication (1944) I stated that among 98 observations of my own 15.7% had a definite neuropathic family history. But inquiries which I have since made into the family histories of normal persons do not encourage me in this view.

The exogenous factors which have been postulated as influencing the pregnant uterus and, thus, contributing to the birth of a Mongol, may be subdivided into A. General exogenous factors: i.e. (1) exhaustion, (2) alcoholism, and (3) syphilis; B. increased amniotic pressure; and C. the theory of nidation.

A. (1) Shuttleworth stated as long ago as 1909 that the Mongol is the product of uterine exhaustion and that the advanced age of the mother, previous frequent child-bearing, also toxic influences leading to reproductive exhaustion, and further exhaustive illnesses of whatever kind during that period of gestation may produce a Mongol.

His views have been widely accepted. Tredgold reported that in a large proportion of cases there was a history of ill-health, privation or anxiety of the mother during gestation.

A number of investigators found or suspected lack of certain vitamins and hormones. Tredgold for example postulated that lack of a hormone or of hormones and vitamins in the mother during pregnancy may cause a certain alteration in the germ chromosomes. It would certainly be worth while to investigate further on these lines though in my opinion the cause is to be found elsewhere.

Stoeltzner reported three cases in which hyperthvroidism in the mother was followed by the birth of Mongoloid children. Lanz experimenting on goats showed that after extirpation of the thyroid gland cretinoid baby goats were born. Geyer in 1937 stated that lack of hormones leads to some damage to the ovum or prevents its maturation.

In a recent publication Benda, Dayton and Prouty suggested that the lack of some hormones which are essential for the development of the fœtus, especially the lack of gonadotrophic, thvrotrophic and chondretrophic hormones during the prenatal period are the factors leading to Mongolism.

According to Lionel Penrose, Mongolism, although in some degree genetically determined, may owe its origin to diminished potency of the secretions of the corpus luteum, i.e. progesterone, which is responsible for the normal embedding of the fertilized ovum into the uterine wall.

(2) *Alcoholism*.—On the available evidence parental alcoholism as a possible cause can be discounted.

(3) *Syphilis*.—Sutherland in 1899 found syphilis in 11 instances out of 25 cases with 3 probables. Babonneix and Blum reported 2 cases of positive syphilis in Mongols. Lind in Australia noted a close association between Mongolism and syphilis and pointed out that miscarriages appear with unusual frequency in women who give birth to Mongols as well as in other congenital mental defective families. Riddell and Stewart postulated that under certain conditions a syphilitic infection of the mother may cause biochemical changes which are ultimately expressed in the physical peculiarities of Mongolism.

B. *The theory of increased amniotic pressure*.—W. M. van der Scheer in an exhaustive review of Mongolian Idiocy published in 1927 grouped the Mongol together with cyclopy, cebocephaly, arhinencephaly and malformations of the palate and said that all these congenital aberrations owed their existence to too narrow an amniotic sac and too high a pressure inside it. Approximately in the sixth or seventh week of embryonic development serious harm is done to the growing foetus. But this author stresses the point that such a pathological amniotic sac or too high a pressure in it are always caused by a wrong implantation of the ovum into an abnormal and unhealthy mucous membrane of the uterus. The predisposing factor, therefore, is the pathological state of the mucosa. He also says that the age and the condition of health of the father have no significance in the causation of the Mongol.

C. *The theory of nidation*.—Aveling in 1874 introduced this term which means: embedding or "nesting" of the impregnated normal ovum into mucous membrane of the uterus. It is well known that during the early period following impregnation the ovum has to rely for its nutrition on the surrounding tissue fluids only, this takes place through osmotic processes without the help of any blood-vessels which develop some time later. It is quite understandable that a mucous membrane having to serve as a nidus for the impregnated ovum must be perfectly intact and healthy in order to guarantee adequate supply to the foetus. If, however, at this early stage of embryonic life, the normal nutrition of the foetus is hampered by any harm done to this mucous membrane, a pathological development of the foetus may follow. This harm may be caused by various factors. Curettage, the prolonged use of deep X-ray irradiation, the irritant action of various abortifacients, the toxin of syphilis and others may lead to considerable changes in the mucosa, and in some cases to sterility, in others to various kinds of mental deficiency including Mongolism.

The influence of abortion, poisoning and other irritants upon the mucosa of the uterus with regard to subsequent pregnancy has been the subject of various investigations (see Doxiades, 1927; Lenz, 1923; Tobler, 1938; and Lereboullet, 1938).

Some time ago my attention was drawn by Professor Nobel to a very interesting publication by Professor Mayerhofer. This author (1940) made inquiries into the histories of the mothers among his well-to-do patients and found that some young mothers not wanting a child used abortifacients or had a curettage performed. When pregnancy occurred afterwards, the first child to be born was a Mongol. He calls these Mongols "Curettage Mongols". He also describes one case where after deep X-ray treatments of the mother which probably caused extensive damage to ovary and uterus a Mongol was born, termed by Mayerhofer "Röntgenmongol".

I reviewed 98 cases of Mongolism (Engler, 1944) and found that in 12 instances, or 12.2%, miscarriages immediately preceded the birth of the Mongol. Some of the miscarriages were due to mechanical intervention, some to abortifacients, one to syphilis, and in some cases mothers were rather vague as to the probable cause of the miscarriage.

During the last year I have had the opportunity of investigating the cases of 24 more Mongolian children with the following results: The mothers of 3 children could not be interviewed, of the remaining 21 cases the mothers of 11 children admitted miscarriage preceding the birth of the Mongol while 10 denied any miscarriage or pathological bleeding. Even if the 3 not interviewed are included in the number of negative cases, the percentage of positive cases would be 45.8%, a very high figure indeed.

The number of patients investigated here is very small and no conclusions should be drawn as far as the percentage is concerned. Taking the mean between my findings in 98 cases and this lot it would come to 18.9%. These figures depend on statements from parents who give information with great unwillingness and diffidence. They are

prepared to admit a miscarriage by accident, but only few of them will co-operate to such an extent that they will admit a curettage or the taking of abortifacients.

Of the 11 cases under consideration, for example, 2 were definitely due to curettage, 2 to the intake of abortifacients, one to a fall, while in 6 cases no reasonable clue could be elicited. Their answers were definitely evasive, very vague and one could not help feeling that the information was incorrect or a deliberate lie.

In the great majority of the cases I have investigated I have met with the same findings: mothers gave birth to normal and healthy children who developed and progressed normally, then a miscarriage occurred, and the next child to be born was a Mongol. A certain time elapsed, the mother became pregnant again and the next child or children were normal and healthy individuals without any neuropathic stigmata. Is it not, therefore, natural to conclude that the intervening miscarriage had brought about a condition in the mucosa of the uterus which eventually proved detrimental to the new human being and resulted in a pathological development?

In the majority of the cases investigated lately confirmation was obtained that between three and six months elapsed between the miscarriage and the following pregnancy. But I have also had several cases under investigation where the interval between the miscarriage and the fresh pregnancy was one year or over. It is, of course, difficult to say how long an irritated and lacerated mucosa requires in order to be restored to normal conditions. Taking into consideration that healing conditions depend on hygiene, treatment, the age of the patient, the number of previous births, exhausting illnesses and so on, we may realize that sometimes many months may elapse before healthy conditions are restored to such an extent that the normal circulation and with it the normal development of the foetus are guaranteed. Generally speaking, the first three to six months following abortion are the critical period during which the implantation of the impregnated ovum into an abnormal mucous membrane of the uterus may in some circumstances lead to Mongolism. In some mothers, especially in those who have given birth to many children prior to the Mongol, or who have suffered or are suffering from ascending infections of the womb or who are in a poor general state of health, the return to normal conditions of the uterine mucosa may be delayed to a considerable extent. Here we may expect the birth of a Mongol to occur one year after the miscarriage or even later.

A great amount of research work will still have to be done until definite proof of miscarriage as the causative agent is established, but I personally have no doubt that a pathological condition of the uterine mucosa immediately preceding the pregnancy is the only cause of Mongolism. This pathological state of the mucosa can be induced by various factors as mentioned already, X-ray irradiations, the use of lead, iodine, phosphorus, quinine, the toxins of syphilis and tuberculosis, acute inflammatory conditions and the irritant action of a number of abortifacients. These factors will in some cases lead to abortion, in others not, but whether they lead to abortion or not, they will alter the normal state of affairs in the mucosa and will severely imperil the nutritional supply to the growing foetus.

As to the influence of age and exhaustion, exhaustive illnesses, lack of vitamins and hormones and other factors which have been postulated as being the causative agents, they certainly contribute to the deficiency in so far as they all exert a more or less important influence upon the uterus, especially during pregnancy. Any factor of any kind that in one way or another is responsible for the normal and unimpeded functioning of the nutritional supply to the foetus, will when out of order contribute to the deficiency. But it should always be born in mind that though they are contributory factors, the fundamental and original basis for the pathological development is the unhealthy state of the uterine mucosa.

The prognosis as to life is bad. Tredgold, Brushfield and Nobel show that many Mongols die in infancy.

Many others succumb in the second or third decade and only very few reach the age of 50 or over.

Of the 29 Mongols who died in our institution 26 of them died of pulmonary complications.

In some of these cases congenital heart disease was found, contributing of course to early death, but only one patient actually died of heart disease.

As Mongols are prone to bronchial catarrhs and, consequently, are an easy prey and succumb to pulmonary tuberculosis, I would suggest that they be examined at regular intervals.

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During the last year I have had the opportunity of investigating the cases of 24 more Mongolian children with the following results: The mothers of 3 children could not be interviewed, of the remaining 21 cases the mothers of 11 children admitted miscarriage preceding the birth of the Mongol while 10 denied any miscarriage or pathological bleeding. Even if the 3 not interviewed are included in the number of negative cases, the percentage of positive cases would be 45.8%, a very high figure indeed.

The number of patients investigated here is very small and no conclusions should be drawn as far as the percentage is concerned. Taking the mean between my findings in 98 cases and this lot it would come to 18.9%. These figures depend on statements from parents who give information with great unwillingness and diffidence. They are

It therefore seems inescapable that, in any discussion of the ætiology of Mongolism, maternal age cannot be ignored, though consideration of the way in which it operates is obviously a problem of extreme complexity especially when it is recalled that about 17% of all Mongols are the first born. Moreover, unless we assume that the effects of maternal age may operate in one pregnancy but not in the next, it is difficult to understand how the birth of a Mongol to an ageing mother can ever be followed by that of normal children, and yet we know that such an event is by no means uncommon.

In his opening remarks, Dr. Engler states that Shuttleworth was the first to point out that the Mongol was the product of uterine exhaustion. I feel that this is rather too generous a tribute to pay to this writer. Uterine exhaustion is a very vague term, difficult to define, and it must certainly be regarded as nothing more than a speculation unsupported by histological evidence.

As Dr. Engler appears to subscribe whole-heartedly to the theory of nidation, I must confess I was a little disappointed to learn that in the series of Mongols investigated by him, a history in the mother of miscarriage or of the use of abortifacients or the curette was found in only 18.9%. It seems to me that this percentage is so low as to render his conclusions statistically invalid; he has also told us that he was dealing with mothers who, to some extent, were not interested in their children and that, if the parents had been unbiased, the figure which he gives would have been far higher. I am a little surprised to learn of this hesitancy on the part of parents, because, in my experience, which I believe is shared by others, the social class of the parents of Mongols is considerably above the average; many belong to skilled artisan and clerical classes and have an intelligence of a superior order.

In statistical surveys of this kind, the question of controls is important and one would like to know whether an investigation of the maternal histories of a group of defectives who were not Mongols would not yield very similar results.

According to Van der Scheer (1919), a history of miscarriages is obtained just as often from the mothers of other types of amentia.

Dr. Engler has expressed the belief that the healing tendency of the uterine tissues may be so slowed down that a long time elapses before normal conditions are restored. A delay of this sort would, it seems to me, favour the multiple incidence of Mongolism, yet we know that, apart from the presence of twins, very few families ever present more than one Mongol.

Since it is implicit in the nidation theory that the lesion must occur during implantation of the fertilized ovum, the study of Mongol twins may be expected to provide data for testing its validity. In this connexion, Jervis (1943) points out that the finding of complete concordance in monozygotic twins is difficult to reconcile with the nidation theory, in fact, when nidation takes place the division of the embryo into twin cell groups has already occurred and the possibility presents itself that one cell group may be affected and the other not, resulting in discordant monozygotic twins. The incidence of discordant monozygotic twins should be of the same order as the incidence of discordant dizygotic twins. Now there are on record at least fifty-eight pairs of discordant dizygotic twins, but incidences of monozygotic twins with one member affected by Mongolism and the other not, have yet to be reported.

My own personal view is that more support could be found for the hypothesis that Mongolism is caused by defective ova, and, although this theory does not harmonize with all the known facts, it is one which deserves more consideration than it has hitherto received.

THE PROGNOSIS OF MONGOLISM

Prognosis can be considered from two aspects (a) the mental and (b) the physical.

(a) Unquestionably the majority of Mongols are in the lower grades of amentia, and their education is therefore largely a problem of habit training. A review of the intelligence quotients of the last fifty Mongols admitted to Leavesden shows that in only one instance does the mental age exceed ten years and that 90% fall in the categories of idiocy and low-grade imbecility.

The single and outstanding example of high grade deficiency in this series is that of a male Mongol now in his 26th year. With an I.Q. of 73 by Burt's modification of the Binet Simon scale, he shows an even better rating with performance tests, and this is reflected by his ability to do excellent work on the manufacture of tooth-brushes. He possesses an excellent memory and, for a mental defective composes quite a good letter. Mongols of so high a grade are, however, quite exceptional and this is the only example I have encountered in more than twenty years' experience of the condition.

(b) Physical prognosis.—It is well known that during the first few years of life the Mongol's death-rate is very high; Brousseau found that 40% died during the first five years of life.

Why this should be so is not very clear, for the investigations of Liebovitz and Yannett (1942) appear to show that the Mongol does not lack the humeral antibodies found in the normal subject.

Congenital heart disease is another contributory cause of the high infantile mortality and there is no doubt that in early adult life Mongols are peculiarly susceptible to pulmonary tuberculosis; possibly their tendency to catarrh of the mucous surfaces predisposes them to this disease.

Statistics of the ages at death of fifty Mongols at Leavesden indicate clearly that a large proportion succumb in early adult life. In this series, 64% died of pulmonary tuberculosis.

However, under modern hygienic conditions, institutional Mongols have acquired a rather better expectation of life and it is becoming not uncommon to see Mongols who have reached the "fifties". A feature of those who survive to middle age is the disappearance of some of the characteristics of Mongolism and the rapid onset of symptoms of premature ageing. Most Mongols in their forties look at least fifteen years older. In

Those among them who are not too low grade, should have some physical training and some light manual work in order to overcome their usual clumsiness and improve their circulation.

The mental prognosis is certainly not good. Though they are excellent mimics and learn to sing correctly, with advancing age they deteriorate to a low grade of imbecility or idiocy. Still, I have come across some fairly high grade Mongols who are doing some useful work under the supervision of intelligent tutors. I am sure that many a Mongol's mental condition could be improved or at least maintained if he was trained efficiently and thoroughly. Much is still to be done for them in this respect.

My purpose in this paper has been to show that many of the older theories have paved the way for my view that the unhealthy condition of the uterine mucosa, caused by various factors, is the only cause of Mongolism.

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Dr. R. M. Stewart: The problem of the causation of Mongolism was debated by members of this Section under the presidency of the late Dr. R. H. Cole in 1926 and I wonder if to-day, after the lapse of nearly two decades, we can claim that there have been any substantial additions to our knowledge of this problem?

On the clinical side progress has been made. We know more about the incidence and distribution of Mongolism, the study of Mongol twins has yielded information useful to the geneticist and something has been gained from biochemical and pathological research. New theories have replaced old ones, but unfortunately as yet none has been advanced which rests on evidence which is susceptible of either clinical or experimental proof. Cretinous animals are easy to produce, but no one has succeeded in producing a mongoloid rat! After listening carefully to the views expressed by Dr. Engler, I am bound to confess that I am left with the belief that the cause of Mongolism still eludes us.

It has long been customary to classify defectives from the ætiological standpoint into primary and secondary groups, denoting respectively, hereditary and environmental causation.

The case for a genetic influence appears to rest largely on the observations that some of the characteristics of the Mongol may be exhibited by parents or by other blood relations, that more than one Mongol may be found in the same sib-ship and that the disease occurs with undue frequency in twins. On the other hand, those who oppose the view that the essential cause is germinal assert, that, according to Mendelian expectation, the larger the family, the greater in it should be the incidence of any given hereditary condition.

Now in the case of the Mongol it is by no means unusual to find that he is one of a large family, of perhaps ten or more siblings, yet even in the largest families the multiple incidence of Mongolism is practically unknown. When more than one is reported, either the Mongols are twins or they are siblings of a relatively small fraternity.

Benda and his co-workers (1943) could find only two examples of multiple incidence in a series of 255 cases; each belonged to a family of three siblings. Furthermore, mental deficiency which is determined by hereditary factors should cause no disturbance of birth order; the primary ament may be expected to occupy any place in the family, he may be the first or the last born or he may occupy any intermediate position, but, as Dr. Engler has mentioned, the position of the Mongol in the family is characteristic—nearly half are the last born and born of mothers whose ages are significantly high. Comparing the ages of 255 mothers of Mongols with those of an equal number of mothers at the birth of defectives who were not Mongols, Benda found striking differences: in the Mongol group 27% of the mothers were over 40, in the second group 3% were over 40.

[January 9, 1945]

War Psychiatry in the Merchant Navy

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Nor so long ago the Merchant Marine, normally a civilian business concern, became the primary objective of the enemy's exertions at sea. So considerable were the resulting casualties in ships that the highest priority was given to their defence and repair. With an unfortunate disregard for skilled man-power the same energy was not shown in repairing the psychological effects of sea warfare amongst officers or men. The study, over fourteen months, of 334 such casualties, of whom 139 were officers and 195 were men, has proved valuable in furthering our knowledge of the traumatic battle casualty and modifying the lessons we hope to carry into the peace.

ÆTIOLOGY

(a) Precipitating factors.

Precipitation of illness often occurred in violent and dramatic circumstances. A consistent severity of trauma was found which it would be unwise to belittle as merely dramatic since, in a majority of patients, it certainly moulded the subsequent reaction. While in respect of a few cases we agree with Blain (1943) in the significance of personal events before, during and after the "battle" episode, in precipitating nervous illness, we found such events generally to be of secondary or minor importance. Over three-quarters of the patients had suffered explosions at sea by torpedoes, mines, bombs or shell-fire, often two or three times, and dated their symptoms from one of these events. Immersion, followed by exposure and semi-starvation in life-boat or raft, and maybe capture by the enemy frequently succeeded the initial explosion. After disablement or destruction of their ship the Merchant Navy have nothing which corresponds to the help of Army Field Ambulance, and only rarely can Air Sea Rescue or Naval Medical Services assist them. It is scarcely surprising that wounded figure little in the Merchant Navy casualty returns. On April 4, 1944, for four years of war there were 30,000 casualties, made up of 26,000 killed (i.e. 1 out of every 8) and 4,000 internees. The number is twice that for the four years of the last war. Other precipitating incidents were collisions, the sight of nearby ships exploding or sinking, the loss of a special friend or the by no means unfounded fear of being trapped when the ship was hit. In fact, in only 3.9% were definite traumatic incidents absent.

(b) Predisposing factors.

In considering personal qualities and events which predispose to breakdown we found a group which collectively was significant.

(1) *The incidence of previous psychiatric illness* 5.5%, agrees with Bellamy (1943) who finds it no higher than in ordinary surgical casualties. By contrast, Craigie (1944) at an Army Psychiatric Centre in the Middle East, reports an incidence of 21.7%.

(2) *The average length of service* for all patients was 10.8 years and the dilution of regular Merchant Navy personnel by those joining for war services only was less than one-third, in the period covered by this paper. Many of these men, therefore, had experience in plenty so far as the essentials of their occupation were concerned.

(3) According to Tooth (1944) in the Royal Navy *domestic stress* was responsible for more invaliding (35.6%), than either enemy action (29%), or conditions of service (22.6%). Domestic stress was a significant factor in causation in 16% of our series, and only 9% of all patients were invalidated for this reason. Occasionally, the domestic situation determined a man's return to sea rather than otherwise.

(4) *Group moral.* Their compliance with the conditions of service at sea, well known to be hard and lacking the amenities of the Forces, contrasted strongly with their lack of toleration of authority in their conduct on shore. Even in peacetime the Merchant Navy was scarcely to be ranked amongst the safer occupations, and its conditions were such that only recently has the practice of offering a choice between prison and the

the female Mongol there does not, however, appear to be a tendency for the menopause to be reached unduly early.

In my experience, endocrine therapy is without influence either on the mental or physical state of the Mongol, but as the majority of my patients have been adults it is possible that less unfavourable results would have been obtained at an earlier age.

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Major Thomas A. Munro, R.A.M.C.: Mongolism is one of the curiosities of medicine. These small gruff-voiced and often placid happy little imbeciles have such a striking appearance that they appear stamped from the same mould and they thus stand out from the heterogeneous mass of mental defectives easy to identify and to the skilled eye recognizable at a glance. The warm-hearted human interest they arouse is perhaps the origin of some of the superficial speculations which have been made about their aetiology. The blood group in cases of Mongolism does not suggest relationship to Asiatic races.

Although Mongolism is the most obvious of all the clinical types of mental defect, minor mongoloid traits occur among other mental defectives. Definite objective clinical criteria are therefore very necessary to make the diagnosis.

Penrose's publications from the Research Department of the Royal Eastern Counties Institution have established facts about the origin of the abnormality.

Familial cases do occur and also cases among more distant relatives. If a mental defective is a case of Mongolism then the chance of finding another case of Mongolism in the family is ten times greater than the chance if the defective is not a case of Mongolism. There is a low incidence of mental defect among parents and siblings. Miscarriages in the sibship are more frequent than in the sibships of other defectives.

It is well known that the incidence of Mongolism increases with maternal age. But there is a greater incidence in pregnancies before the age of 25 than between the ages of 25 and 29 years. There is a high incidence of miscarriages and infantile deaths just where there is a high incidence of Mongolism.

At the Royal Eastern Counties Institution, 5% of Mongols were born premature and 10% of cases were cases of threatened abortion. Miscarriages and deaths in infancy among the sibs are more frequent than average. The mortality of Mongols in the R.E.C. Institution is six times greater than that in the general population. It seems likely, therefore, that when due allowance is made for these environmental factors, the incidence of Mongolism is very much higher in affected sibships than is usually supposed. The observed familial incidence is 1.9%. If the rate of miscarriages and infantile deaths among Mongols be taken to be nine times greater than the average, then the estimated incidence of Mongolism in sibships rises towards 25%. It is considerations such as these which suggest that another factor in the causation of Mongolism is a genetic factor, in action irregularly dominant.

The President: During the past forty-five years I have seen over 2,000 cases of Mongolism. It has not, of course, been possible to make an adequate investigation of all these; but I have done so in a considerable number, and I have observed some of them over periods of from twenty to thirty years. The condition appears to be such a distinctive entity that it might reasonably be expected to be the result of some one particular cause, and that this cause would be readily ascertainable. Actually, however, the question of causation is full of difficulties and paradoxes.

As Dr. N. Burke has pointed out, although the great majority of Mongols are easily recognized, there are many defectives who are not Mongols but who present some of the features of this condition, and these are known as "semi-Mongols". In fact, I think there is hardly a single feature of Mongolism which I have not seen in ordinary defectives and some of them are found in normal persons. With regard to the theory of nidation, as pointed out by Major Munro there is great need for control observations, and I have made some attempt to obtain these by inquiring of several of my gynaecological colleagues. All of them tell me that curettage is one of the commonest operations performed upon women and that they have never noticed it to be followed by any special incidence of Mongolism. Also, inquiries which I have made on this point of the mothers of Mongol children have failed to reveal any abnormal amount of curettage, miscarriages or uterine disease.

I do not think we know with certainty whether the cause lies in the germ or the environment of the fertilized ovum. At one time I was inclined to think the latter; but since then the number of instances in which more than one Mongol has occurred in the family, the fact that where both twins have been Mongols they have in all probability been monovular, and that where one has been a Mongol and the other normal they have been binovular, has led me to think that the cause lies in the condition of the germ cell. My present view is that Mongolism is in all probability due to a pathological impairment of the germ before fertilization consequent on a temporary hormone or vitamin deficiency of the mother. I fully admit, however, that this is merely a hypothesis, and I agree with Dr. R. M. Stewart that the cause of Mongolism is still an unsolved riddle.

There is one other point regarding prognosis which has not been mentioned. It is that while epilepsy is exceedingly rare in Mongolism, mental disorder is by no means uncommon. I have seen a number of these patients suffering from anxiety states and hysteria, and some who have presented the characteristic features of progressive dementia præcox.

and in some of our cases had done so, are not incompatible with many years at sea in the Merchant Navy in war or peace. With the type of man who volunteers for sea under present conditions screening out the abnormal personalities by psychiatric examination is likely to be relatively ineffective unless these special considerations are taken into account.

(8) Lack of group sense and the scheme of organization of the Merchant Marine share responsibility for the situation that often arises between captains and crews. The captain legally represents the ship's company, not the interests of the men, who naturally tend to rely on their Union in such matters. In their relations with the captain too often the crew are wondering what his motives are, rather than considering it possible for him to do them a disinterested service. This relationship of employer and employed still colours the men's attitude in war, so that attempts at better discipline are viewed as an unnecessary brake on their roving propensities or as entailing loss of rights instead of a means of improving their own efficiency.

(9) Amongst other potent factors in predisposition must be considered the *anticipation of danger*. Occasionally it is sufficiently acute to be a predisposing influence, especially amongst engineers, radio officers and those on duty in closed compartments on or below deck. The engineer may regard his engine room as a coffin but the deck as a place of comparative security. The naval practice of relaying information from time to time to various parts of the ship during enemy action is of value in easing psychological tension. Knowledge of a difficult situation can usually be tolerated better than ignorance, leaving a fearful imagination full play. There is no doubt that the prolonged tension experienced by rather more than half of all cases undermined their ability to adjust to the excessive fear response that assailed them in real emergency.

(10) *Occupation*.—Investigation into the way the various occupations on ship affected the incidence of breakdown, indicated in the officer group, that radio officers in proportion to their numerical strength on ship had the most psychiatric casualties. In war theirs is an unsatisfactory lot, owing to the radio silence observed at sea. They have little to do and sometimes help out the other officers in minor ways. They mostly work under enclosed conditions, and by comparison they are the least skilled of the officer group. The executive officers on deck showed the lowest incidence (22·8%).

In other ranks stewards ranked highest with an incidence of breakdown of 16·8%, cooks, able seamen and firemen followed in decreasing order of incidence.

Generally speaking those on deck showed a lower incidence than those working below or in closed spaces.

(11) *Antecedent illness*.—The most prevalent illnesses considered to have lowered the patients' resistance to nervous breakdown were malaria 9·3%, fevers of the enteric group 2·2% and peptic ulcer 2%.

As regards other factors: All but 14% attained top standard at school. Psychiatric abnormalities appeared in the near relatives of 20% of cases.

In summarizing our conclusions concerning aetiology we believe that the excessive preponderance of anxiety and depression especially the former to have been the result of the considerable trauma experienced or the mere association with dangerous environments.

This trauma, or the anticipation of it, had changed for these men the character of an environment which had thus far served as a refuge from a maladjusted life on land.

They were faced, not only with the development of war neurosis, but placed in the quandary of having to revert to the scenes of former failure. They had failed both at sea and ashore, hence the persistent anxiety, hostile attitude towards authorities, unsettled behaviour in hospital and at home, and the difficulty of rehabilitation afterwards. It is highly probable that some of these men will return to sea as soon as the war is over.

DIAGNOSIS

Anxiety states	227	67·9%
Depressions	37	11·1%
Hysterias	27	8·0%
Psychopathic states	14	4·2%
Schizophrenias	9	2·9%
Post-traumatic—Anxiety	5	1·4%
—Depression	2	0·6%
Neurasthenia and exhaustion	4	1·2%
Obsessional neurosis	1	0·3%
Epilepsy	2	0·6%
Post encephalitis	2	0·6%
Senile dementia	1	0·3%
Malingering	1	0·3%
G.P.I.	1	0·3%
Myasthenia gravis	1	0·3%

Merchant Navy ceased in the courts. Not until May 1, 1944, could a man take annual leave without loss of pay, since pay formerly continued only when "operational". In peacetime Shipping Companies endeavoured to promote successful integration of crews by keeping them together for several trips, since a single voyage may be nearly over before the crew begin to settle as a unit. Under the present pool system it is not uncommon for a man to change ships at the end of each trip, especially if leave is taken, yet there was little resentment at this change. How different is all this from the group sense cultivated in the warship, the regiment and the R.A.F.

(5) *Without previous training for war* the merchant seaman has to ply his vital business against an enemy-infested sea, and to face aggression under conditions of relative personal and collective inactivity, with meagre chance of retaliation, in civilian craft which till the later stages of the war could only be afforded modest escort.

(6) *Sexual abnormalities*, generally speaking, were conspicuous by their absence; sexual inadequacy occurred in 6.5%, but no sexual perversions were recorded. Their inadequate emotional attitude may have made the patients more fitted for sea life but went against them when faced again with the home situation. Half our series were married. In the Army the majority are married.

(7) The above considerations are all associated with our conclusions concerning the personality of the Merchant seaman. The Merchant Navy is recruited on a voluntary basis and it is axiomatic that to some extent the job selects the man. A diversity in quality of officers and men is apparent—a not unexpected corollary of the varied motives, at least superficially, for going to sea. Inquiry into the reason for the choice of a seafaring life showed that while a quarter selected the sea as their form of war service for the duration many, on casual inquiry, said they chose it for adventure, to see the world, because they fancied it, or because of family tradition. More careful questioning made it clear that a great majority chose it as an escape for their restless, emotionally shallow personalities, personalities which were always living in the near future and seeking out the next move, a restlessness besides which their hard service conditions seemed to them of lesser account. As a group they were intolerant of control, individualistic, lacking group sense and making few friends except possibly for one special pal, on whom they became over-dependent. At sea they may long for the home port, but once there they show little tendency to stay, soon signing on for another ship. Their superficial adjustment to sex assists them to tolerate long periods afloat. Thus, one way and another, the Merchant marine provides an adjustment for this type of personality. Hence the long average service, 10.8 years, low incidence of previous psychiatric illness, low incidence of invaliding for domestic stress, compliance with adverse conditions of work, good or satisfactory work record in all but 10%.

While this type of personality adjusts fairly well in peacetime, it is susceptible to breakdown under the severe anxiety and fear provided by the traumatic experiences of sea warfare; but breakdown means return to the very environment in which previously they had failed to adjust, and from which escape had been sought at sea. Consequently, we find much delay in reporting sick and tendency to return to sea "to cure themselves".

If unable to return to sea, they displayed feelings of inferiority, of suspicion, a sense of grievance for supposed ill-treatment and in general a tendency to an irritable paranoid state. In hospital as soon as symptomatic relief had occurred, there was a liability to take their own discharge or to misconduct themselves with a view to getting it. 6.7% left the hospital in this way and in American reports (Bellamy, 1943) 22%. At home, where many were unfortunately sent for long periods, their unsettled conduct and irritability produced constantly recurring histories of domestic discord, in which the patient was frequently aware of his unworthy share. While their early hospital treatment was no special problem, their subsequent rehabilitation was distinctly difficult.

By ordinary psychiatric criteria, 46.5% of the whole series showed personalities which, prior to their illness, could be adjudged mildly or grossly abnormal, mainly the former. The duration of service in the abnormal personality group averaged 7.3 years as opposed to 11.1 years in those personalities considered normal. Anxious and depressive states predominated in those having a normal personality (93.6%), rather than in the abnormal where the incidence dropped to 70%. So far as duration of war service only was concerned, there was little difference between the normal and abnormal personality groups, being 2.86 years in the former and 2.76 years of war in the latter. Evidently, numerous abnormal personalities stood the difficulties of their occupation very well and many suffered multiple traumatic incidents, though occasionally a single torpedoing with or without much attendant personal hardship terminated all attempts to adjust at sea, and perhaps provided the avenue of escape from it. It is fairly certain that abnormal personality traits, which might lead to rejection from the fighting Services

and in some of our cases had done so, are not incompatible with many years at sea in the Merchant Navy in war or peace. With the type of man who volunteers for sea under present conditions screening out the abnormal personalities by psychiatric examination is likely to be relatively ineffective unless these special considerations are taken into account.

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DIAGNOSIS			
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—Depression	2
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Obsessional neurosis	1
Epilepsy	2
Post encephalitis	2
Senile dementia	1
Malingering	1
G.P.I.	1
Myasthenia gravis	1
			334
			100

Merchant Navy ceased in the courts. Not until May 1, 1944, could a man take annual leave without loss of pay, since pay formerly continued only when "operational". In peacetime Shipping Companies endeavoured to promote successful integration of crews by keeping them together for several trips, since a single voyage may be nearly over before the crew begin to settle as a unit. Under the present pool system it is not uncommon for a man to change ships at the end of each trip, especially if leave is taken, yet there was little resentment at this change. How different is all this from the group sense cultivated in the warship, the regiment and the R.A.F.

(5) *Without previous training for war* the merchant seaman has to ply his vital business across an enemy-infested sea, and to face aggression under conditions of relative personal and collective inactivity, with meagre chance of retaliation, in civilian craft which till the later stages of the war could only be afforded modest escort.

(6) *Sexual abnormalities*, generally speaking, were conspicuous by their absence; sexual inadequacy occurred in 6.5%, but no sexual perversions were recorded. Their inadequate emotional attitude may have made the patients more fitted for sea life but went against them when faced again with the home situation. Half our series were married. In the Army the majority are married.

(7) The above considerations are all associated with our conclusions concerning the personality of the Merchant seaman. The Merchant Navy is recruited on a voluntary basis and it is axiomatic that to some extent the job selects the man. A diversity in quality of officers and men is apparent—a not unexpected corollary of the varied motives, at least superficially, for going to sea. Inquiry into the reason for the choice of a seafaring life showed that while a quarter selected the sea as their form of war service for the duration many, on casual inquiry, said they chose it for adventure, to see the world, because they fancied it, or because of family tradition. More careful questioning made it clear that a great majority chose it as an escape for their restless, emotionally shallow personalities, personalities which were always living in the near future and seeking out the next move, a restlessness besides which their hard service conditions seemed to them of lesser account. As a group they were intolerant of control, individualistic, lacking group sense and making few friends except possibly for one special pal, on whom they became over-dependent. At sea they may long for the home port, but once there they show little tendency to stay, soon signing on for another ship. Their superficial adjustment to sex assists them to tolerate long periods afloat. Thus, one way and another, the Merchant marine provides an adjustment for this type of personality. Hence the long average service, 10.8 years, low incidence of previous psychiatric illness, low incidence of invaliding for domestic stress, compliance with adverse conditions of work, good or satisfactory work record in all but 10%.

While this type of personality adjusts fairly well in peacetime, it is susceptible to breakdown under the severe anxiety and fear provided by the traumatic experiences of sea warfare; but breakdown means return to the very environment in which previously they had failed to adjust, and from which escape had been sought at sea. Consequently, we find much delay in reporting sick and tendency to return to sea "to cure themselves".

If unable to return to sea, they displayed feelings of inferiority, of suspicion, a sense of grievance for supposed ill-treatment and in general a tendency to an irritable paranoid state. In hospital as soon as symptomatic relief had occurred, there was a liability to take their own discharge or to misconduct themselves with a view to getting it. 6.7% left the hospital in this way and in American reports (Bellamy, 1943) 22%. At home, where many were unfortunately sent for long periods, their unsettled conduct and irritability produced constantly recurring histories of domestic discord, in which the patient was frequently aware of his unworthy share. While their early hospital treatment was no special problem, their subsequent rehabilitation was distinctly difficult.

By ordinary psychiatric criteria, 46.5% of the whole series showed personalities which, prior to their illness, could be adjudged mildly or grossly abnormal, mainly the former. The duration of service in the abnormal personality group averaged 7.3 years as opposed to 11.1 years in those personalities considered normal. Anxious and depressive states predominated in those having a normal personality (93.6%), rather than in the abnormal where the incidence dropped to 70%. So far as duration of war service only was concerned, there was little difference between the normal and abnormal personality groups, being 2.86 years in the former and 2.76 years of war in the latter. Evidently, numerous abnormal personalities stood the difficulties of their occupation very well and many suffered multiple traumatic incidents, though occasionally a single torpedoing with or without much attendant personal hardship terminated all attempts to adjust at sea, and perhaps provided the avenue of escape from it. It is fairly certain that abnormal personality traits, which might lead to rejection from the fighting Services

and in some of our cases had done so, are not incompatible with many years at sea in the Merchant Navy in war or peace. With the type of man who volunteers for sea under present conditions screening out the abnormal personalities by psychiatric examination is likely to be relatively ineffective unless these special considerations are taken into account.

(8) Lack of group sense and the scheme of organization of the Merchant Marine share responsibility for the situation that often arises between captains and crews. The captain legally represents the ship's company, not the interests of the men, who naturally tend to rely on their Union in such matters. In their relations with the captain too often the crew are wondering what his motives are, rather than considering it possible for him to do them a disinterested service. This relationship of employer and employed still colours the men's attitude in war, so that attempts at better discipline are viewed as an unnecessary brake on their roving propensities or as entailing loss of rights instead of a means of improving their own efficiency.

(9) Amongst other potent factors in predisposition must be considered the *anticipation of danger*. Occasionally it is sufficiently acute to be a predisposing influence, especially amongst engineers, radio officers and those on duty in closed compartments on or below deck. The engineer may regard his engine room as a coffin but the deck as a place of comparative security. The naval practice of relaying information from time to time to various parts of the ship during enemy action is of value in easing psychological tension. Knowledge of a difficult situation can usually be tolerated better than ignorance, leaving a fearful imagination full play. There is no doubt that the prolonged tension experienced by rather more than half of all cases undermined their ability to adjust to the excessive fear response that assailed them in real emergency.

(10) *Occupation*.—Investigation into the way the various occupations on ship affected the incidence of breakdown, indicated in the officer group, that radio officers in proportion to their numerical strength on ship had the most psychiatric casualties. In war theirs is an unsatisfactory lot, owing to the radio silence observed at sea. They have little to do and sometimes help out the other officers in minor ways. They mostly work under enclosed conditions, and by comparison they are the least skilled of the officer group. The executive officers on deck showed the lowest incidence (22·8%).

In other ranks stewards ranked highest with an incidence of breakdown of 16·8%, cooks, able seamen and firemen followed in decreasing order of incidence.

Generally speaking those on deck showed a lower incidence than those working below or in closed spaces.

(11) *Antecedent illness*.—The most prevalent illnesses considered to have lowered the patients' resistance to nervous breakdown were malaria 9·3%, fevers of the enteric group 2·2% and peptic ulcer 2%.

As regards other factors: All but 14% attained top standard at school. Psychiatric abnormalities appeared in the near relatives of 20% of cases.

In summarizing our conclusions concerning aetiology we believe that the excessive preponderance of anxiety and depression especially the former to have been the result of the considerable trauma experienced or the mere association with dangerous environments.

This trauma, or the anticipation of it, had changed for these men the character of an environment which had thus far served as a refuge from a maladjusted life on land.

They were faced, not only with the development of war neurosis, but placed in the quandary of having to revert to the scenes of former failure. They had failed both at sea and ashore, hence the persistent anxiety, hostile attitude towards authorities, unsettled behaviour in hospital and at home, and the difficulty of rehabilitation afterwards. It is highly probable that some of these men will return to sea as soon as the war is over.

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G.P.I.	1
Myasthenia gravis	1
			334
			67·9%
			11·1%
			8·0%
			4·2%
			2·9%
			1·4%
			0·6%
			1·2%
			0·3%
			0·6%
			0·6%
			0·3%
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			0·3%

SYMPTOMATOLOGY

The bias in symptoms already mentioned shows itself in the following diagnostic groupings. States of anxiety 67.9% and depression 11.1% tended to occur together. To decide which should have the primary diagnostic label was sometimes difficult. States of hysteria 8% and psychopathic behaviour 4.2% were frequently complicated by anxious and depressive trends. The unusual preponderance of anxiety and depression made symptoms somewhat standardized. Psychological and somatic manifestations of fear were most evident in the form of sleeplessness, nightmares, irritability sometimes followed by sensations of guilt or remorse, restlessness, feelings of weakness, lassitude, and of "tension in the head". More purely somatic symptoms such as headache, various aches and pains, diarrhoea, frequency of micturition, tremors, gastric discomfort, nausea or vomiting, dizziness, palpitations, liability to be startled unduly by sudden noises and a lowered tolerance to alcohol were also observed.

In more recent cases the prevailing response was an exaggerated physiological fear reaction with prominent autonomic instability. Unfortunately the average duration of illness before admission was 14.3 months by which time the autonomic aspect of the case had become moulded and fixed in a neurosis with considerable depression and anxiety, presenting a formidable therapeutic problem so far as return to sea was concerned. States of anxiety and depression tended to be mixed and difficult to differentiate so that the common clinical picture was that of an anxious depressive reaction, with weakness and irritability, occurring in men of varied previous personality, physique, education and training. In this they resembled, at least initially, the exhaustion states of operational Service units. These exaggerated but fundamentally physiological responses usually started while at sea, and at times necessitated temporary absence from duty but for the most part symptoms were largely smothered until return to port where a more florid state of neurosis ensued, due partly to faulty self-interpretation of symptoms, and partly because as Curran and Garmann (1944) have pointed out a heightened sense of tension and awareness which is appropriate at sea becomes incongruous and a nuisance ashore under a reduced tempo of living. At home the neurotic picture changes. Free anxiety is reduced while feelings of resentment and paranoid ideas of criticism by the family tend to intrude. This is understandable if one remembers the poor personality adjustment to civilian domestic life. Until recently treatment facilities were inadequate. Consequently the men felt neglected at home and their resentment increased.

It has been obvious that the greater the actual traumatic stress the more nearly do the clinical findings present a uniform standard picture. Constant and continued stress is less well tolerated than short attacks of great severity, e.g. Pearl Harbour produced relatively few neurotic casualties compared with Guadalcanal or Dunkirk.

Motor hysterical manifestations were rare, conditions at sea make conversion hysteria a very unprofitable compromise. In the anxiety states it cannot be said that in the Merchant Navy the predominance of such states was due to wider recognition of such conditions as has been suggested elsewhere. Symptoms were usually fully developed, and early recognition was exceptional, before specialist treatment was sought so far as our particular experience goes. As regards alcohol, a fair amount of symptomatic drinking occurred though probably not in excess of Service patients. The chronic drunkard was rarely diagnosed and part of the alcoholism encountered was certainly due to the diminished tolerance associated with neurosis.

Physical examinations showed that over 50% of patients had lost from a half to three stones in weight, 12% had abnormally high blood-pressure chiefly due to anxiety, while active or latent syphilis, bronchitis, arteriosclerosis and vitamin deficiency, each occurred in under 3% of cases. The significance of persistent loss of weight in war neuroses has been discussed by Sargant and Craske (1941) as an indication of the effort made by the patient to overcome his neurosis and the need for the use of a modified insulin regime.

TREATMENT

Treatment is difficult in view of the previous adjustment at sea except in the very young and the elderly. The former are usually more willing to leave the sea and can be directed into training schemes in industry. The latter can be retired. The chief difficulty comes when the somatic symptoms of anxiety have been alleviated and the problem of adaptation, of restarting a man on a life he rejected when younger is

presented. Therefore in-patient treatment is incomplete unless it leads to guidance into a new adjustment, obviously not easy in the face of the personality outlined and its unsettled conduct. The following situation is fairly typical: fourteen months before admission the patient was torpedoed and underwent traumatic experiences. Reaching land he had adequate physical first aid, after which he spent from one to three months returning to this country. He made efforts to suppress his symptoms by "working them off" with employment on another ship. Arriving at a home port he was not medically examined and his complaint of illness was met by a direction home under the local general practitioner's care. Under war conditions it was difficult for the latter to prescribe other than mild sedation and rest. Now some patients undoubtedly recovered or improved spontaneously under a convalescent regime or home environment. We met some of those who did not, who instead of improving became more anxious, irritable and unsettled so that relatives noticed their erratic conduct and complained of their altered personality. Financial stringency and sometimes six to twelve months of inactivity generally resulted in the Ministry of Pensions being consulted and ultimately their admission to the special unit for the Merchant Navy at this hospital, where many arrived in a somewhat frustrated, sceptical and unco-operative frame of mind as a result of these experiences. Such were the men whom we aimed firstly to return to sea or otherwise rehabilitate for work of national importance ashore.

In view of this attitude it was very necessary to apply prompt and full clinical examination and early symptomatic relief to secure the patient's co-operation. In the large majority of patients of the anxiety-depression group, where tension tended to be severe, such relief could be obtained by the use of sedation in varying depths and by courses of modified insulin. Adequate quantities of sedative by reducing psychological tension brought considerable symptomatic relief even in some relatively long-standing cases of illness. What is really adequate for such states is generally underestimated. The most useful drugs for this purpose were sodium amytal or phenobarbitone, up to 3 grains four-hourly of the former and 2 grains t.d.s. of the latter being well tolerated by ambulant patients. In severe states of tension and anxiety, continuous sleep was given under sodium amytal 6 to 12 grains four-hourly, for one to three weeks. The method is safe provided experienced medical and nursing staff are available. A vitamin supplement, particularly B₂ complex, is useful since hyporiboflavinosis has occasionally been seen. High-potency yeast tablets, 3 t.d.s., are an effective prophylactic.

Since half these patients had lost from half to three stones weight, and improvement by psychological means is generally delayed until the normal weight is restored, we endeavoured to stimulate metabolism and appetite, and to generate a sense of well-being rapidly, by using modified insulin, Sargent (1941) and Sands (1944a). Furthermore we found progress quicker and safer if, where much tension and loss of weight co-existed, sleep and insulin were combined (Sands, 1944b).

Where hysterical symptoms and loss of weight were severe, anxiety being absent or slight, modified insulin became the primary physical treatment and sedation played a minor role. By the use of these methods which are equally applicable to civilian neurosis (Sands, 1943) progress is much more rapid since the time required for psychotherapy is considerably cut down. Such symptomatic improvement and gain in rapport is liable to be temporary, or short of the best result attainable in any given patient unless adaptation is reinforced by psychological methods.

The physical and psychological treatments are applied in a complementary fashion, so that the physical prepares the constitution for the psychological approach, which in turn stabilizes and furthers progress already initiated.

Generally speaking neither the patient nor his illness could have benefited by analytical psychotherapy had it been economically possible. The types of psychotherapy most useful were found to be abreaction, explanation and such reorientation of ideas as was necessary. For abreaction the lighter periods of continuous sleep treatment were often useful, otherwise a temporary intravenous barbiturate narcosis was induced as first used by Bleckwenn (1930).

In explanation of their illness numerous patients required some instruction on the psychic and physical effects of fear and anxiety. Some had interpreted their somatic symptoms as physical disease of one sort or another, or had developed intractable phobias of such illness. Frequent terrifying nightmares had led some to fear imminent insanity, in others loss of sexual desire engendered dread of chronic personality change. Many more required explanation of their faulty conditioning to experiences afloat and

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lessen the incidence and facilitate the treatment of neurotic illness. These conditions have not occurred in the Merchant Marine because individuals tend to take up the life for their own psychological adaptation and because the commercial lines of the organization are not intended for war. None the less there are other factors which contribute to this disparity in results which could be readily improved. Such factors are:

Avoidable delay in treatment.

One of us made special inquiry into 150 patients to ascertain to what extent this factor had occurred. It averaged six months in this series when assessed from the time each man arrived at a home port and presented himself for medical examination. The delay in some cases has been as long as three years. This means that a man, say a deck officer, trained to carry out a very specialized duty which can have no counterpart in civilian employment may, if he breaks down and is unable to return to sea, present a very difficult problem in rehabilitation. In most cases he is too old for training and we have seen second officers become night watchmen after invaliding. Particularly in conversion hysteria does this delay have serious significance. In fact a man who has been on 100% pension for more than two years for a conversion hysterical syndrome has been in our experience practically untreatable. Treatment in these patients can only be directed to rehabilitation for employment at a very much lower grade of social efficiency. Resentment against authorities and an attitude of chronic invalidism invariably co-exist. Such patients do not differ in any way from other chronic hysterics in which the compensation factor is predominant, but a study of the previous history and circumstances of these cases does not show evidence of previous maladjustment or neurotic illness.

As our results show, in anxiety states, particularly in this type of man, delay in giving treatment is again a serious factor in altering prognosis, because the pattern of his life has broken by breakdown at sea. Men have been discharged from the Service within a few weeks of presenting themselves to the Merchant Pool Doctor, a circumstance which often proved the greatest trauma of all. Fifty-eight of our patients were permanently discharged and four temporarily, before treatment was given. They were then sent home to be under the care of their local doctors. In this way men with long experience at sea, little or no experience of civilian employment, but in a state of nervous illness find themselves faced with financial stringency, and the necessity for starting a new life in a setting from which they had previously fled. Not unnaturally they develop resentment towards the Merchant Navy Pool or Shipping Authorities whom they believe to have treated them in a cavalier manner. If permanently discharged the work which they can obtain, since they have not trained for civilian employment is necessarily relatively unremunerative, and very frequently by precipitating an increase in neurotic symptoms, loss of employment results. The larger number of patients were sent home to the care of their local doctor with neurotic or psychotic symptoms which were too active for recovery with a convalescent regime. Others were sent to the Merchant Navy Convalescent Home but for the same reason had subsequently to be transferred to hospital after a delay which should have been avoidable. It appears that in many instances no pension is given until these men have demonstrated their incapacity for work, and it is only when this is complete that they are admitted to a neurosis centre. Another factor determining the differences between Merchant and Royal Navy personnel is the *absence of any form of selection in the Merchant Navy*. There are, however, some personalities, mildly abnormal by ordinary standards, who do quite well at sea.

Unnecessary stress in conditions of service.

These include lack of adequate rest or leave ashore between periods of duty at sea, only possible because of the acquiescence of the type of personality concerned. Recently it has been possible for reasonable leave to be taken without financial loss. Most of our cases occurred before this change was made. In spite of the presence of active nervous illness 77 of our patients had been returned to sea without treatment, presumably to attempt to "work it off". Their subsequent presence in hospital is sufficient comment on this method of treatment by "passing the buck" to the captain. It merely resulted in further incapacity and resentment by the patient. Formerly patients were sent to hospital without allowances being made to their families so that unless savings were available it often happened that discharge had to be granted before the conclusion of treatment in order that the patient might earn money in the first available job. Fortunately this difficulty has been lessened though not yet overcome.

Attention has been given to possible methods by which these difficulties could be obviated. From experience not only with Merchant seamen but with neurosis in other Services that is our firm opinion, supported by the results of treatment in North Africa and other places, that the prognosis in anxiety states can be completely altered if they are treated as medical emergencies. If this is not done social and psychological factors enter in which initially were unrelated to the neurosis but which can completely change the outcome.

Conditions at sea in the Merchant Marine more or less preclude effective first aid or early treatment, though for years alcohol has been used for this purpose. Its use varies in different ships according to the ideas of the captain and in any event its action is somewhat uncertain. Its effect in moderate dosage is mainly that of a cortical depressant, a doubtful aid where one's safety may depend on rapid intellectual adaptation, and where the symptoms are chiefly of thalamic and autonomic type. In theory and in practice sodium amylal is far more effective. It spares the patient from excessive emotion and prevents fear impairing his performance. Its administration by a senior officer in restricted dosage of say 3 grains morning and evening in acute cases until medical attention is available is worth consideration. In this connexion the work of Heath and Powdermaker (1944) is of interest. Their experience of war neurosis

to associated stimuli on land. Many had been decorated for meritorious war service and they felt ashamed and depressed by their patent jumpiness at sharp noises, the sound of friendly aircraft or air-raid alerts. Not unnaturally this led to much self-consciousness and sense of uselessness.

After months of introspective anxious rumination, no little psychological reorientation towards the problem of their occupation was required. To return to sea was at times a terrifying prospect, and in the face of severe feelings of this nature it was useless to persuade or insist that they should go. They feared repetition of horrifying sights and experiences which no amount of discussion would alter. Others expressed their quandary and failure by proclaiming the iniquities of the officers, of the shipping authorities, or accusing the crew of hindering the war effort, saying the country was rotten; and in general developing a loosely built system of paranoid ideas. We found that such symptoms were often reduced by the initial physical treatment and did not prove to be the obstinate psychotherapeutic problem customarily found in peacetime. None the less, where an aggressive psychopathic constitution was linked with such paranoid thinking it was necessary in a few instances to discharge patients home for misconduct (2.2%) or to the observation ward (3.8%) for further hospital care.

Shock treatment such as insulin comas for schizophrenias and electrically induced fits for depression were employed as required. We would emphasize that good control of patients having E.C.T. is necessary since we noted that while out on pass from the hospital small indulgence in alcohol frequently resulted in aggressive confused states which materially retarded the patient's progress and disturbed the *moral* of the ward generally. Such schizophrenias as occurred usually had little direct precipitation by war stress. Depression was much more common but mainly of superficial reactive type or secondary to anxiety. Consequently E.C.T. was less often indicated than is usual when this condition is endogenous or is the dominating persistent pathological response.

Like some other specialized professions Merchant Navy men are very prone "to talk shop" and to tell of their various fearful war experiences, which while it may act as an abreaction for the narrator, is pregnant with painful associations for others, and, if unchecked, may prejudice progress. For this reason and to provide confidence and social adjustment, patients were encouraged to use auxiliary methods of treatment in occupational therapy units, daily physical training and recreational programmes.

If permanent or temporary discharge from the Merchant Navy was indicated we used our liaison with the Ministry of Labour to recommend suitable employment for men on leaving hospital. Patients interviewed the Ministry's special representative while still in hospital, and for therapeutic reasons the decision regarding disposal was made as early as the circumstances of the individual patient allowed.

RESULTS

In a total of 323 patients 13.3% recovered, 39.6% were much improved, 34.1% improved and in 13% there was no change. Their disposal resulted in 15% being recommended to return to sea, temporary release from seagoing duty in 12.8% for periods varying from three to twelve months, while 61.7% were permanently discharged unfit for sea. 6.7% were discharged for misconduct, against medical advice, as absconded, or at their own request. 3.8% were sent to Mental Homes or Observation Wards. Of the whole group 5.9% were unfit for work on sea or shore at the time of discharge.

U.S. Rest Centres report 57% recommended for sea (Bellamy, 1943), but the type of patient is not entirely comparable since long-standing psychoneuroses, psychopathic personalities, chronic alcoholism and psychosis were excluded from their series. A fair number of the first and second of these groups, and a few of the last were admitted to our hospital unit.

COMMENT

It might be thought that, because the responsibility of the work is often considerable, and there is little chance of psychiatric treatment at sea, that much caution was necessary in recommending return to duty, yet follow-up results indicate that this is not necessarily the right policy. We feel that there should not be so wide a difference between the number of anxiety states returned to sea in the Navy, 90% (Garmany, 1944), and in the Merchant Marine, 25%. In part these differences are the outcome of the purposes for which these Services exist. One effect of the Navy's scheme of training and discipline is the welding of an efficient social group, the ship's company, which will stand the stress of war even when diluted nine to ten times (*The Times*, 14.9.44). Such methods

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DISCUSSION

Dr. E. L. Caldwell-Smith: The problem of psychoneurosis in the Merchant Navy is receiving much consideration from those concerned and there have recently been conferences between the Federation, the Ministry of Health and Ministry of War Transport, on this subject, particularly as to how suitable cases can be brought under proper treatment with a minimum amount of delay. There are, however, many difficulties. The men are civilians, independent by nature, and as a rule dislike Institutional treatment. They are discharged from ships usually not complaining of their symptoms and proceed to their homes, often long distances away from the nearest Reserve Pool, and then come under the care of their panel doctors.

Discharges from the Merchant Navy for nervous diseases are higher than in any other group. During a period (which must be unspecified) out of 9,858 discharges on health grounds 2,163 were for nervous diseases, 21.8%. Of these, as far as can be estimated from available returns 2.4% were for organic diseases of the nervous system including epilepsy, and 19.4% for psychoneuroses and mental diseases, i.e. approximately 1 in 5 of all discharges. As regards incidence, out of 6,437 recent cases of unfitness for seafaring 70 (1.09%) were organic disease and epilepsy, and 523 (8.13%) were psychoneurotic and mental. Difficulty in getting these cases properly treated at an early stage was admitted. One of the main troubles was that on discharge at the end of a voyage or on return to this country after a discharge abroad, the men are paid off at Mercantile Marine Office and proceed to their homes on leave. It was then and during this period that so many cases developed their nervous symptoms and came under the care of their own doctor. Federation and Pool doctors could not interfere and letters and messages to the man's doctor were not productive of their doctor taking active steps as a rule. Federation and Pool doctors would do all they could to assist in getting these men properly treated but with the very large number of cases it was impossible to refer all to psychiatrists and so many treated and reported fit when subsequently sent back to sea relapsed on first voyage and had to be discharged.

At the last conference with the Ministries concerned on this subject certain decisions were reached and it was agreed that when the man was first seen by a Pool doctor and considered curable and likely to be fit for seafaring again the Pool doctor would send the man to the nearest psychiatrist on a list to be provided by Ministry of Health who would put the necessary machinery in motion to get the man admitted to a suitable Institution.

Dr. M. N. Pai: A discussion on Merchant Navy Psychiatry would be incomplete if no mention were made of the incidence of psychiatric disorders among Asiatic seamen especially Indians who, since the outbreak of war, have played their part magnificently and in every respect worthy of the highest traditions of the British merchant marine. In spite of educational and cultural disadvantages, linguistic difficulties and problems such as insecurity of tenure and consequent financial instability, religious customs and personal habits they have stood up to intense enemy action at sea remarkably well indeed. Even in heavily "blitzed" cities like Liverpool and Cardiff the psychiatric casualties among Indian seamen have been negligible. This is a tribute to the average Indian seaman's constitution which can apparently withstand any amount of stress without abnormal psychological reactions—a fact which is not generally known. One would like to hear the views of doctors who look after Indian seamen and perhaps Dr. Sands could tell us what percentage of his patients were Asiatic seamen and whether he has any comment to make on psychiatric disorders among them.

Dr. Karl Evang (Director-General of the Norwegian Public Health Services): During the war, sailors of the merchant fleets have been working under an extremely severe pressure. Mentally they are not protected by the fact that they belong to an organized body like a military organization, and they have not the advantage of co-operating and fighting together with the same persons for a long time. They also have no way of fighting back, and therefore have very little natural outlet for their aggression towards the enemy. I am not a psychiatrist myself, but have had an opportunity to get in contact with these problems through the Norwegian Public Health Service which has been set up for the benefit of Norwegian men in this country, the United States of America, Canada and India.

We have been struck by the very few cases of what might be called traumatic war neuroses among Norwegian sailors during the war. The medical superintendent at one of our convalescent homes, reported that during one year about 24,000 Norwegian crew members visited a certain harbour. During the same year 296 Norwegian sailors were

amongst Merchant seamen at a United States Rest Centre has also led them to believe that in recent cases of "battle reaction" one is dealing with physiological type of response in the form of an exaggerated expression of fear, and they endeavoured to make treatment specific by the use of ergot, the sympathetic depressant, in addition to psychotherapy. Very encouraging results were obtained in the twenty cases reported.

In addition to such early measures, it would be preferable in order to avoid delay in treatment ashore, that when a man is declared unfit in the absence of adequate physical cause, he should be referred forthwith to a psychiatrist. At present he is usually the last doctor a patient sees. It is appreciated that in some parts this is not an easy matter, but in Liverpool, Cardiff, Bristol, Glasgow, Newcastle and London where the majority of such patients are, this should present no difficulty. In these towns there are psychiatric out-patient departments at general hospitals and the services of local E.M.S. psychiatrists are available. We believe that prompt treatment within a day or two of return to port, such as occurs in other Services would bring about a substantial improvement in results, diminish invalidism and expense to the country in pensions and allowances. To reap the full benefit of early treatment it is necessary to support it with greater care in the selection of officers and men and to dispose of some of the aggravations noted in this paper. As in the Navy, good conditions of service and the fostering of a sound group spirit constitute not only the best prophylactic measures against neurosis but are most valuable in promoting early recovery from such illness.

RESULTS OF TREATMENT IN 187 CASES FOLLOWED UP FROM SIX TO EIGHTEEN MONTHS

	At discharge 323 cases	Followed up 6 to 18 months 187 cases
Recovered	43 13.3%	15 8.0%
Much improved	128 39.6%	106 56.7%
Slightly improved	110 34.1%	20 10.7%
No change	42 13.0%	46 24.6%

PRESENT EMPLOYMENT IN 147 CASES FOLLOWED UP FROM SIX TO EIGHTEEN MONTHS

STATUS		DISTRIBUTION	
Rise	0	Shore	116
Equal	118	Sea	25
Lower	16	River	3
Unknown	4	Canal	1
UNEMPLOYED	40	Army	2
Including	3 in hospital 3 awaiting ship 1, Government Training Scheme.		

Follow-up Results

A total of 187 reports are available. Results of treatment show that the "slightly improved" group has tended to sort itself out into a definite state of improvement or relapse. The net result being that in the long run 64% of patients were substantially benefited. The earning ability of those in employment was maintained, as a rule, on shore. Nearly a quarter were still unemployed, more than half being clinically in the unchanged group.

The outcome on the 55 men recommended to return to sea is of some interest. Of these we know that 16 directed to sea stayed on shore, that 19 did in fact return to sea together with 6 others not recommended to do so. The minimum number at sea is therefore 25. However we know that 20 more were recommended to return to sea and of these 15 who had the follow-up questionnaire sent to them did not reply, so that the follow-up netted just over two-thirds of the possible replies. While the number of those certainly at sea is 25 or 13%, and if one takes these figures as guides, then it is highly probable that the actual number at sea is approximately 31 or 16.5%.

Incidentally 6 out of 187 (3%) returned to sea against advice and this is the minimum figure. We have never heard of a discharged soldier doing this, but such returns against advice are a likely result in the type of personality described.

SUMMARY

These 334 officers and men of the Merchant Marine have demonstrated the psychiatric aspect of their service. Besides this they are in effect, a control series which typify the unfortunate results of delay in treating traumatic illness whether this has occurred for reasons which are or are not beyond control. Such delay while often fatal to further service at sea is not necessarily prejudicial to success on shore if suitable rehabilitation is employed.

Though active warfare may cease to be a relevant factor, those Merchant seamen driven ashore by its stress, will in some instances and despite all effort to the contrary fail to readjust on land. To avoid much anti-social conduct it may be necessary to get these men back to sea at the close of hostilities.

We would like to thank Dr. Louis Minski, Medical Superintendent of Sutton Emergency Hospital, for permission to publish the case materials for this paper.

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DISCUSSION

Dr. E. L. Caldwell-Smith: The problem of psychoneurosis in the Merchant Navy is receiving much consideration from those concerned and there have recently been conferences between the Federation, the Ministry of Health and Ministry of War Transport, on this subject, particularly as to how suitable cases can be brought under proper treatment with a minimum amount of delay. There are, however, many difficulties. The men are civilians, independent by nature, and as a rule dislike Institutional treatment. They are discharged from ships usually not complaining of their symptoms and proceed to their homes, often long distances away from the nearest Reserve Pool, and then come under the care of their panel doctors.

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signed off at the same harbour after having been torpedoed. In that year 60 psychiatric cases were admitted to the convalescent home which was the only one admitting Norwegian patients of this type. Half of these cases were not pertinent to our problems to-day. In the remaining group an obvious connexion with the war situation was found in only about half of the group, 15 men. One of the reasons why cases of this type have occurred relatively seldom in the Norwegian Merchant Navy during the war may be that the Norwegian merchant men also in peacetime are accustomed to being away from their families and their country for long periods, often several years at a time. They would also, of course, as a group, constitute experienced sailors who have been working in the same profession for a long time.

As a prophylactic, the Norwegian Government has tried, in all large harbours where there are manning pools for the Allied fleets, and also in several smaller harbours, to establish necessary medical and social services for the men.

Dr. Sands: Replying to Dr. Pai, the number of Asiatics in our series was only two. There were three Africans and nine Europeans of various nationalities. In view of the theme developed in this paper, it is very doubtful if the domestic background and the factors operable in civil life, which we have described, apply to Asiatics. Such information as I have suggests that when Asiatics break down they do so shortly after the traumatic event, whereas in the group discussed the breakdown tended to occur at the home port and to be cumulative with time.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[December 21, 1944]

FOUR CASES PREVIOUSLY SHOWN

Two Cases of Multiple Arsenical Cutaneous Carcinomata.—BRIAN F. RUSSELL, M.D., and ROBERT KLABER, M.D.

THE PRESIDENT: Apropos of multiple skin tags of the neck (October Meeting *Proc. R. Soc. Med.*, 1945, 38, 128), there is an American article by H. J. Templeton in *Arch. Derm. Syph.*, Chicago, 1936, 33, 495, in which he came to the conclusion that the tags in question in middle-aged women were not warts and were not fibromas and he suggested the name "Cutaneous Tags of the Neck". However I have a case now under my care at Wellhouse Hospital in a girl aged 28 who has tags on her neck which are obviously pedunculated warts and she has a large number of plane warts on her chin.

Occupational Argyria.—J. E. M. WIGLEY, M.B., and P. M. DEVILLE, M.D.

THE PRESIDENT: Another point I wish to mention is that when Dr. Wigley showed a case of argyria at the May meeting (*Proc. R. Soc. Med.*, 1944, 37, 648) I referred to a paper by Firth and Harrison (*Brit. J. Derm.*, 1924, 36, 105). I said at the time that I thought Firth and Harrison had found a deposit of silver "in the epidermis". Dr. Harrison has since called my attention to the fact that in their case there was no deposit of silver in the skin except in the basement membrane of the sweat glands and sweat ducts and here and there in the sebaceous glands but none in the epidermis.

Lichen Planus.—LOUIS FORMAN, M.D.

W. M., aged 40, male. An engineer. He was shown at the November 1944 meeting under the provisional diagnosis of lichen planus. He first came to hospital in May 1944, when the condition had been present for two and a half years. There were infiltrated, red, scaling patches in front of the ears, on the forehead, and on the upper lip. The scale was easily detached and showed horny projections from the under surface, suggesting lupus erythematosus.

Biopsy from the skin in front of the ear was made in May 1944. There was a well-defined granular layer and dilated follicular orifices filled with horn. In the papillae there were collections of lymphocytes; the lower margin of the infiltrate was well defined, and the lymph vessels were dilated. The microscopic appearances were more suggestive of lichen planus.

On May 17, 1944, blood W.R. and K.R. were negative. In July 1944 five weekly injections of 0.01 g. of myocrisin were given. He was seen again on November 1, 1944, when he showed ulceration of the mouth, scaling macules on the limbs and trunk, and papules over the trunk very suggestive of lichen planus. The stomatitis and general eruption had appeared ten weeks after the injections of gold. The areas over the lip and forehead were more infiltrated and scaly.

It had been suggested by various members at the November meeting that the patient had secondary specific disease, and a small healing ulcer was demonstrated on the penis. There was enlargement of the inguinal glands. The eruption has faded during the past three weeks and the ulcer healed within a week. To-day small papules are to be seen on the penis. The papular lesions on the chin are flatter and shiny. The original areas on the forehead and cheeks are less raised.

The blood reports on November 22 and 29, December 6 and January 3 were W.R. and K.R. negative.

It would appear that this patient had a generalized lichen planus or a toxic lichenoid eruption precipitated by the gold injections.

Atavistic Pigmentation.—F. E. GRAHAM-BONNALIE, M.B. (Introduced by Dr. JOHN FRANKLIN.)

Woman, aged 36. She was quite normal until the winter of 1942-43, when she noticed, on going out into the cold, that her face smarted, and in the summer the skin began to irritate and peel especially around the eyes, and pigmentation started and spread more or less all over the face. Her blood-pressure is normal. She was told that she had some "black blood" in her, and then discovered for the first time that her grandfather was a negro. She is now typically negroid in appearance. The interesting points are whether this should be accepted as permanent and why signs of pigmentation did not occur before the age of 34.

The President: We have had a number of cases of pigmentation of the face and elsewhere recently, and I do not think we have arrived at a diagnosis of any of them, but so far as I know, none of the patients had negro or negroid ancestors. This woman has a definitely negroid facies.

Dr. F. Parkes Weber: At all events provisionally we must, I suppose, accept this case as one in which the cutaneous pigmentation in a person of negroid ancestry developed late. In doubtful cases of pigmentation in the mucous membrane of the mouth it has repeatedly been suggested and more or less accepted that if no other cause can be found and there is some cause in the ancestry (such as Mediterranean or negroid blood), the ancestry must be accepted as being the cause of the oral pigmentation. Cutaneous pigmentation, is, to my mind, far more likely to occur than oral, and provisionally in the present case one must accept the ancestry as the cause of the cutaneous pigmentation. The pigmentation must be supposed to have been present potentially in the genes of the zygote, though not obviously present in the skin at birth. It required some exposure to bring it out, and the facial exposure has in this case brought it out on the face. The characteristic racial hair was present at birth, but the pigmentation of the face was only potentially present. I think that explanation to be more than plausible, but it is not certain, and the follow-up of the case may show that it is wrong.

Major A. Neish Barker, R.A.M.C.: I saw this woman about nine months ago working at the A.T.S. training depot, where she was doing a good deal of outdoor work, drilling the girls and so forth, and I thought her face was rather negroid, but the pigmentation was not so marked as now—it was more *café au lait*. I asked her about it, and she told me about her grandfather. When I wrote to the doctor I suggested that she should be transferred to a unit where she would not be quite so much exposed. I lost sight of her until this afternoon; she now tells me she has been transferred to the R.A.S.C. The condition was a little scaly when I saw her first.

Dr. Louis Forman: This patient has had attacks of soreness and chapping of the face with oedema, particularly of the lower eyelids. Such a reaction might be due to an external irritant. She uses a face cream at night. She would be liable to pigment strongly after such attacks of dermatitis owing to her inheritance.

Major N. M. Wrong, R.C.A.M.C.: I believe that if these cases were atavistic we should see a number of them in the United States, where there are many half-castes and quadroons and so on. But I have never seen nor heard of one.

Dr. H. S. Stannus: This woman has some pigmentation in the nails which I think points to racial origin. I might point out that a negro baby at first though pigmented is paler than the adult. The degree of pigmentation of the adult may depend a good deal on climate. A native working in the deep gold mines of South Africa under conditions of heat and damp—not of sunlight—will change from a chocolate brown to coal black. There is obviously a great ability to develop pigment in such races.

Dr. Parkes Weber: Does that apply to dark people in general—to the dark people of any race, including the white races?

Dr. Stannus: I think so.

The President: It is interesting that the heat in South African mines should be more powerful than the sun.

Dr. Stannus: Heat plus high humidity as water is used in drilling the quartz rock.

? **Atypical Erythema Annulare Centrifugum.**—G. B. DOWLING, M.D.

Woman, aged 28, married, in good general health and with no past history of illness of any importance.

About a year ago she developed an area of rather dark red erythema in front of the right knee. Thereafter other lesions appeared gradually, about a dozen of them altogether, scattered chiefly on the limbs. Some are faintly red, others almost the colour of the skin generally; all with the exception of the original lesion on the knee are rather firm flat elevations; in some the margin appears to be raised above the rest of the lesion and there is quite a close resemblance to granuloma annulare. Apart from the far larger area on the knee, the size of the patches varies from about that of a sixpence to a florin.

Histologically there is nothing remarkable to be seen; the changes consist of patchy infiltration of the dermis with inflammatory cells, sometimes rather dense and chiefly situated about blood-vessels.

The condition differs from erythema annulare in the persistence over a really long period of each lesion; not one has disappeared or regressed to any appreciable extent; neither has there been any tendency to alter in shape. Both sarcoid and granuloma annulare are excluded by the histology. The Wassermann and Kahn reactions are negative.

For those who believe in a series of cutaneous reactions ranging from erythema annulare centrifugum (Darier) at one end to granuloma annulare at the other, this type would appear intermediate. I think it is perhaps a somewhat atypical example of erythema annulare.

The President: It seems to me much more like granuloma annulare, especially the lesions on the forearm.

Dr. Dowling: I agree, but there is nothing characteristic of granuloma annulare in the patch on the knee.

Dr. W. Freudenthal: I think the biopsy lends some support to granuloma annulare.

Dr. Dowling: The section was taken from a lesion on the thigh. There was no sign of necrosis.

POSTSCRIPT (16.3.45).—Since the case was presented her lesions have become far more annular and larger.—G. B. D.

Infantile Acne.—W. N. GOLDSMITH, M.D.

M. K., boy, aged 6 months. First seen November 30, 1944.

On examination.—On the prominences of both cheeks and the chin are red papulopustules. On close examination a few tiny blackheads can be seen.

History.—Since birth; intermittent; non-pruritic. Mother had bromides during pregnancy and fed the baby for his first three months. Mother's brother is tuberculous.

Investigations.—Cultures from four of the pustules (the contents were cheesy rather than frankly purulent) gave *Staphylococcus aureus*, coagulase +, from two, the other two being sterile. Mantoux-1:10,000 was negative, as was also a tuberculin paste, both being applied to an affected area and to normal skin.

Comment.—The condition is mentioned by Leiner in "Jadassohn's Handbuch". He says that in newborn cases the condition clears up in a few weeks. This has lasted six months. Aitken has published several cases of infantile acne and reviews the literature in the *Brit. J. Derm.*, 1942, 54, 272. From this it appears that the pustular form noticed at birth or soon after is exceedingly rare. This is rather surprising in view of other seborrhœic manifestations in the newborn, presumably under the influence of maternal gonadal hormones.

The President: Is the mother still taking bromides?

Dr. Goldsmith: No. I may add that the condition is said to have gone up and down a little, but I have observed it for six weeks and it has shown no change.

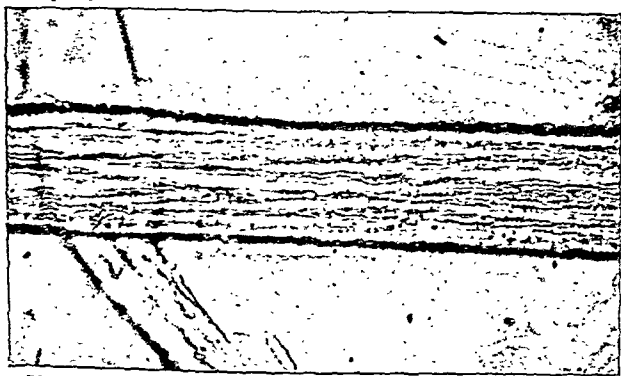
Favus.—C. H. WHITTLE, M.D.

D. F., a boy, aged 6½ years.

The child comes from a Barnardo's Home, is an evacuee, and the history is uncertain. The eruption, of probably more than six months' duration, consists of adherent heaped-up scales on the scalp in discs varying up to one inch in diameter. The scales are rather matted together, the result of a 'serous exudate, which can be seen when the mass of scales is forcibly removed: there are left moist, red, circular, sharply defined areas of skin, and the removal causes pain. There are no obvious broken hairs or scutula. There is some sign of bald areas developing. The lesions are mostly around the crown of the head, but there has been a circular, scaly, red disc on the open skin of the nape of the neck.

I wrote "psoriasis" as the diagnosis in the out-patient department, confirmed by absence of fluorescence under Wood's light. Fortunately I also took scales and hairs for microscopy, and some of these were found when examined later in the day to contain abundant fungus elements, chiefly coarse branching hyphæ. A few infected hairs showed slight fluorescence only. An infected portion of hair shaft also showed the characteristic fungus inside the shaft, with the still more characteristic air tubules. Cultures on Sabouraud's maltose agar show early colonies of what I think is *Achorion schoenleinii*.¹

The case is shown because of the ease with which it may be mistaken for psoriasis and/or sepsis. Such "atypical" cases of favus are not uncommon. I have two other similar cases details of which I hope to publish. These cases are so like psoriasis that one must expect to examine many cases which are not favus in order to catch the few that are.



Photomicrograph of hair showing long hyphæ within the shaft. × 180.

The President: I suppose it is not a mouse fungus by any chance?

Dr. Whittle: That is an interesting point, but judging from the two previous cases that I have had—which were proved by culture to be of human type—I would regard this as another case of human origin. Cultures should settle the question, and I will report results.

The President: Do favus-infected hairs normally fluoresce much?

Dr. Whittle: An American authority on the subject says that they usually do (Lewis, G. M., and Hopper, Mary E., "Introduction to Medical Mycology", 1943, second edition, p. 274, Chicago), and the two other cases which I had earlier this year certainly fluoresced brilliantly. In one, a girl, the infected hairs came down to the shoulders, and

¹ Confirmed by Dr. J. T. Duncan.

fluoresced throughout their length. I had failed to diagnose the first case until a second child became infected by contact. However, I take comfort in the fact that this case was missed by at least three London dermatologists.

Dr. W. N. Goldsmith: In the cases of favus I showed recently I failed on two occasions to find any fungus by direct examination. The culture was *Achorion schoenleinii*. Fluorescence was variable.

The President: That was apart from anything being put on them?

Dr. Goldsmith: Yes.

The President: These were cases of atrophic bald areas?

Dr. Goldsmith: Yes, in the mother: the child had no baldness yet.

Dr. Louis Forman: Dr. Dowling also thought that Dr. Goldsmith's patient had favus. He demonstrated to me many years ago a rather similar case of atrophic folliculitis which he diagnosed as favus. This was a Turkish woman who had been in this country for some fifteen years.

Hæmorrhagic Telangiectasia.—C. H. WHITTLE, M.D.

R. H., a man aged 35.

History of two and a half years of small hæmorrhagic spots in the skin and mucous membrane of the mouth, together with occasional nose-bleeding. There are pin-head-sized, or slightly larger, bluish-red angiomatous tumours dotted about on the cheeks, lower lip, tongue, buccal surface of cheeks, fauces, tonsil, and the skin of the back of the left hand. Some of these have been hæmorrhagic, and extravasated blood was seen around the lesion.

Bleeding time, clotting time and capillary resistance test (Hess) were normal; the platelets 160,000 per 5 million red cells (normal).

Family history.—No history of similar trouble obtained. In spite of no known family history this case should be classed in the group of hereditary telangiectasia described by Sutton in 1864, Rendu (1896), Osler (1901), and Parkes Weber (1907), as mentioned by Wintrobe (*"Clinical Hæmatology"*, 1942, published by Henry Kimpton, London).

Dr. F. Parkes Weber: Although a great many cases of this condition have been shown at various times in London, I think we are greatly indebted to Dr. Whittle for having brought forward this particular case. There are many differences between the different cases, and different cases show special points. Various special points are connected with this case. This is a case of an otherwise perfectly healthy man with cutaneous and mucosal telangiectases and a history of recurrent nose-bleeding. If one examines him fairly carefully one may be absolutely certain that the case is one of this "Osler" type of telangiectasia, because it will be found that under some of the nails, and showing through them, there are also very small (streaky) telangiectases. That combination of telangiectases occurs, as far as I know, in no other disease or syndrome whatever, and no other question need be asked about it in order to make the diagnosis.

A second point is that this patient appears always to have had a tendency to recurrent epistaxis. There are cases of familial epistaxis in which obvious cutaneous telangiectases never develop, and yet from family history or otherwise one may be sure that they belong to the Osler group. In the present case, if we had seen the patient some years ago, we would have found no obvious telangiectases whatever; he is quite sure about that. He was born with almost congenital epistaxis, but the telangiectasia was also potentially present in the genes of the zygote.

The third point is that the patient tells us that he had on one occasion hæmaturia. He says that he passed this sanguineous urine after eating many strawberries.

A fourth point is the absence of any history pointing to heredity. Dr. Whittle has the choice of regarding his patient as the first member of the family to manifest this disease in the family though their existence cannot be ascertained in the ordinary course of questioning.

Lupus Verrucosus.—P. J. FEENY, M.B.

K. C.-K., aged 23. Lesion on dorsum of right hand and fingers.

History.—Two and a half years ago had amputation above the right knee-joint for tuberculosis of the joint. Tubercle bacilli had been found on aspiration. Eighteen months ago, developed a fungiform warty growth the size of a sixpence over the second right metacarpophalangeal joint. This growth was completely excised and sectioned. Over a year later the present eruption appeared at the site of the section, and it spread peripherally while tending to clear at the centre. A biopsy was made, and serial sections were examined. A large portion of the affected skin was then excised for further investigation. At the suggestion of the pathologist, Dr. W. W. Woods, this was cut into pieces, each piece was embedded in paraffin and sections from each block were made.

Demonstration.—All the above-mentioned sections were shown. Individual endothelial cells and one or two giant-cells of the Langhans' type were present in all the sections. One piece from the middle of the large portion of excised skin yielded sections showing a typical lupus nodule. Such a tubercle system was not seen in any of the other sections.

Dr. F. Parkes Weber said that the case was clinically typical.

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Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[December 1, 1944]

DISCUSSION ON ANÆSTHESIA IN THE DENTAL CHAIR

Dr. K. B. Pinson : *Cyclopropane*.—There are attractive features in cyclopropane anæsthesia for dental surgery and other mouth operations: quietude, good oxygenation, and early and often phenomenal relaxation of the jaw.

There are two ways of administering cyclopropane—one with, the other without, CO₂ absorption.

The normal method is with absorption. It is suitable both for adults and children, particularly for cases which cannot well be managed with intravenous barbiturate alone. Intubation is almost a *sine qua non* for dental work. The method is in general unsuited to the dental surgery, however, as the cases are too long, recovery too slow, pre-operative medication is indicated, and so on. There are some cases of children with multiple fillings, done in the dental chair, and taking an hour or two or even longer, where I feel it is the only fitting method. Even with young children of 7 or 8, it goes extremely well and I have done it many times. Cavities are cleared and synthetic and amalgam fillings completed, with any necessary extractions.

The second method is applicable only to children because CO₂ absorption can be dispensed with only where the accumulation of CO₂ in the breathing bag is slow. It is eminently successful but some of the lesser shortcomings of cyclopropane remain. At the Stretford Dental School Clinic I rely mainly on other methods and reserve cyclopropane for that minority of cases where young children need extractions which are likely to take more than the usual minute or two.

The apparatus is simple and has been described in the *Brit. Med. J.* of April 29, 1944, p. 588. It consists of a rubber measuring bag of 1 pint capacity, filled from the cyclopropane cylinder, the gas being pumped by a Higginson's syringe into the breathing bag which has been first half-filled with oxygen. This breathing bag, of two or three gallons capacity, is fixed on to the chair and connected direct to the valveless nose-piece by as short a length of flexible wide-bore tubing as possible. It is also simple to use.

The method seems capable of being reduced to a formula or rule of thumb to a greater degree than others, which may have its appeal. Induction takes a little longer than with N₂O but is quite smooth, there being no struggling and the children generally not moving at all. The nose-piece is applied, and for the first breath or two they inhale only oxygen, breathing back into the bag. Cyclopropane is now gradually added by squeezing the rubber syringe, at first slowly and then more quickly, until three pints have been added. Small children may be managed with 2½ pints. Operating begins as soon as they are under or the jaw relaxed. A gag is as a rule not used, and this instrument is very gladly avoided.

The tranquil breathing lessens any tendency for blood to reach the larynx; in every case we have had sufficient operating time, and the depression of respiration which is a feature of cyclopropane is not too much in evidence. This is owing to the anæsthesia never being deep.

There is one particular danger which must only be realized, to be easily combated. Children sometimes salivate rather profusely. Should the saliva reach the larynx and induce a degree of spasm, this, with the enfeebled respiratory effort, may soon bring about a serious degree of anoxia. One soon learns, however, by careful induction and head position, to prevent this occurrence, and it could presumably be circumvented by atropine, given as a routine beforehand. We do not do this, and the only case of trouble occurred early on in our work.

I believe there is no sudden toxic or unexplained danger in the use of cyclopropane. Following are the features which deter us from making first choice this otherwise most satisfactory anæsthesia: (1) The time is limited generally to three or four minutes;

fluoresced throughout their length. I had failed to diagnose the first case until a second child became infected by contact. However, I take comfort in the fact that this case was missed by at least three London dermatologists.

Dr. W. N. Goldsmith: In the cases of favus I showed recently I failed on two occasions to find any fungus by direct examination. The culture was *Achorion schoenleinii*. Fluorescence was variable.

The President: That was apart from anything being put on them?

Dr. Goldsmith: Yes.

The President: These were cases of atrophic bald areas?

Dr. Goldsmith: Yes, in the mother: the child had no baldness yet.

Dr. Louis Forman: Dr. Dowling also thought that Dr. Goldsmith's patient had favus. He demonstrated to me many years ago a rather similar case of atrophic folliculitis which he diagnosed as favus. This was a Turkish woman who had been in this country for some fifteen years.

Hæmorrhagic Telangiectasia.—C. H. WHITTLE, M.D.

R. H., a man aged 35.

History of two and a half years of small hæmorrhagic spots in the skin and mucous membrane of the mouth, together with occasional nose-bleeding. There are pin-head-sized, or slightly larger, bluish-red angiomatous tumours dotted about on the cheeks, lower lip, tongue, buccal surface of cheeks, fauces, tonsil, and the skin of the back of the left hand. Some of these have been hæmorrhagic, and extravasated blood was seen around the lesion.

Bleeding time, clotting time and capillary resistance test (Hess) were normal; the platelets 160,000 per 5 million red cells (normal).

Family history.—No history of similar trouble obtained. In spite of no known family history this case should be classed in the group of hereditary telangiectasia described by Sutton in 1864, Rendu (1896), Osler (1901), and Parkes Weber (1907), as mentioned by Wintrobe (*"Clinical Hæmatology"*, 1942, published by Henry Kimpton, London).

Dr. F. Parkes Weber: Although a great many cases of this condition have been shown at various times in London, I think we are greatly indebted to Dr. Whittle for having brought forward this particular case. There are many differences between the different cases, and different cases show special points. Various special points are connected with this case. This is a case of an otherwise perfectly healthy man with cutaneous and mucosal telangiectases and a history of recurrent nose-bleeding. If one examines him fairly carefully one may be absolutely certain that the case is one of this "Osler" type of telangiectasia, because it will be found that under some of the nails, and showing through them, there are also very small (streaky) telangiectases. That combination of telangiectases occurs, as far as I know, in no other disease or syndrome whatever, and no other question need be asked about it in order to make the diagnosis.

A second point is that this patient appears always to have had a tendency to recurrent epistaxis. There are cases of familial epistaxis in which obvious cutaneous telangiectases never develop, and yet from family history or otherwise one may be sure that they belong to the Osler group. In the present case, if we had seen the patient some years ago, we would have found no obvious telangiectases whatever; he is quite sure about that. He was born with almost congenital epistaxis, but the telangiectasia was also potentially present in the genes of the zygote.

The third point is that the patient tells us that he had on one occasion hæmaturia. He says that he passed this sanguineous urine after eating many strawberries.

A fourth point is the absence of any history pointing to heredity. Dr. Whittle has the choice of regarding his patient as the first member of the family to manifest this mutational gene disease or he may suppose that there were previous instances of the disease in the family though their existence cannot be ascertained in the ordinary course of questioning.

Lupus Verrucosus.—P. J. FEENY, M.B.

K. C-K., aged 23. Lesion on dorsum of right hand and fingers.

History.—Two and a half years ago had amputation above the right knee-joint for tuberculosis of the joint. Tubercle bacilli had been found on aspiration. Eighteen months ago, developed a fungiform warty growth the size of a sixpence over the second right metacarpophalangeal joint. This growth was completely excised and sectioned. Over a year later the present eruption appeared at the site of the section, and it spread peripherally while tending to clear at the centre. A biopsy was made, and serial sections were examined. A large portion of the affected skin was then excised for further investigation. At the suggestion of the pathologist, Dr. W. W. Woods, this was cut into pieces, each piece was embedded in paraffin and sections from each block were made.

Demonstration.—All the above-mentioned sections were shown. Individual endothelial cells and one or two giant-cells of the Langhans' type were present in all the sections. One piece from the middle of the large portion of excised skin yielded sections showing a typical lupus nodule. Such a tubercle system was not seen in any of the other sections.

Dr. F. Parkes Weber said that the case was clinically typical.

Dr. Feeny, in reply, said that the case was being shown in order to draw attention to the need for a careful laboratory technique. It was unwise to rely on just serial sections from the same block. Although the diagnosis in this case could be made from the preliminary sections, one might easily cut away the whole block without finding what one should find, thereby missing the diagnosis and having no block left.

When the needle is in the vein, the first $\frac{1}{2}$ c.c. is injected very slowly. This is to make sure that the needle is intravenous and not intra-arterial. The patient will give ample warning of intra-arterial injection by complaining of an intense burning pain shooting down the arm.

The next 2 to 3 c.c. are given moderately fast and if the patient is not asleep at this stage (that is after about 3 c.c.) a pause is made in the injection for about thirty seconds. Only a very few unpremedicated adults will be asleep on less than this small amount. If at the end of the pause the patient is still conscious, another cubic centimetre is given and a further pause made—and so on until loss of facial expression, muscular relaxation and regular automatic respiration show that third stage anæsthesia has been reached. Then a further amount of pentothal is injected rapidly. Precisely how much depends on the sleep dose already given and on the expected duration of the surgical procedure. If only a very short anæsthesia is required, I inject rapidly a quantity up to half the sleep dose already given. For longer operations an amount equivalent to the sleep dose may be given in this rapid injection. The needle is then withdrawn and the oral pack is introduced.

Supplementary nasal gas and oxygen is next administered. The reasons for supplementing are (1) From his position at the back of the patient the anæsthetist can support the jaw and thereby maintain the freedom of the airway. He can also be of great help to the dentist by providing counter-pressure against the thrust of his forceps and thereby make for stability of the head and jaw. (2) The adjuvant effect of nitrous oxide makes it possible to use minimal quantities of pentothal. In this way the post-operative recovery period is cut to a minimum. Actually if this technique be used, the majority of patients awake when the gas is stopped as quickly as if they had N_2O only. (3) Extra oxygen can easily be given—a great help to those patients with cardiac or respiratory disease, or those in whom the pentothal has been sufficient to depress the respiration.

Dr. A. D. Marston : *Nitrous oxide and oxygen by nasal inhalation.*—The first recorded use of nitrous oxide as an anæsthetic agent for dental extraction in the chair occurred on December 11, 1844, in the town of Hartford, Connecticut, U.S.A. The anæsthetist was Mr. Colton, described by Buxton (1900) as an itinerant lecturer in chemistry, the patient was the famous Dr. Horace Wells, and the dental surgeon was Mr. Biggs. However, the actual discovery and perfection of the gas took place in this country through the work of Priestley, Humphry Davy and Michael Faraday.

Provided anoxia is avoided and efforts at securing muscular relaxation are not overstressed, then of all anæsthetic agents nitrous oxide is the least toxic and the least harmful to the normal working of the human body (Langton Hower, 1944).

Nitrous oxide and oxygen are employed in the dental chair mainly for healthy adolescents or adults who require an average duration of anæsthesia lasting from two to six minutes for the removal of one or more teeth.

Premedication is not usually required, but in cases of anxiety—and some otherwise healthy people dread any induction of anæsthesia—premedication is a distinct advantage. For adults I usually prescribe two tablets of allonal at bedtime on the night before operation, and two more one hour before administration of the anæsthetic. For children I use small doses of seconal which are given at the same times. Suitably premedicated subjects are not only more amenable to narcosis but the basal metabolic rate being lowered less oxygen is required and the anæsthetist's task is thus clinically simplified.

The patient should arrive at the dental surgeon's house some ten minutes before operation so that the bladder may be evacuated and a few quiet moments be spent before entering the surgery. He is then shown to the dental chair and it is explained to him that the best way of taking gas is to relax all the muscles, to close the eyes, and to breathe naturally through the nose.

Posture.—The patient must sit well back in the chair, the head being in line with the body which should be as vertical as possible to the chair, the hands loosely clasped in the lap, and the feet and legs either drawn up or else on the floor or hanging towards the floor on either side of the foot-rest. Although a pelvic strap is used by many anæsthetists, I find that I can manage without this, and reserve it only for cases with a turbulent past history.

Procedure.—The anæsthetist should always inquire which teeth are to be extracted, whether any exceptional difficulty is likely to be encountered, and in which order the teeth are to be removed. As soon as the mouth prop has been inserted by the dental surgeon, the anæsthetist should commence the administration without delay.

The nose-piece is applied gradually, and a moderate and silent flow of pure nitrous oxide is presented. At the same time the anæsthetist talks quietly to his patient, encouraging him to relax all muscles and to breathe gently through the nose. The expiratory

(2) There is no reliable analgesia as they come round. (3) In the period of recovery children come round more slowly than from N_2O , and have to be carried to the anteroom; where they are then able to sit at a basin. (4) Sickness is the chief drawback: of the first 500 cases 21% were sick.

There are a few other minor after-effects, such as irritability, roughness, drowsiness and pallor, lasting only a short time. Two children were noted as feeling poorly and one stayed two hours before going home. Some difficult cases were successfully dealt with, the method being deliberately chosen.

Dr. F. W. Roberts : Pentothal.—From the dental point of view the criticisms which can fairly be levelled against pentothal are two: First, with the heightened irritability of the larynx and the possibility of local manipulations and debris causing an effective stimulus, there is a risk of a troublesome, if not actually dangerous, spasm of the larynx.

Secondly, the recovery period from intravenous anaesthesia—even pentothal which is the most quickly detoxicated of the barbiturates—is more prolonged than from the usual quick dental gas, which is extremely rapid.

These disadvantages can be very effectively counteracted by posturè, minimal dosage and supplementary nitrous oxide oxygen analgesia.

The advantages to be gained by the use of pentothal in selected cases in the dental chair are:

(1) A rapid pleasant induction of third stage anaesthesia. (2) The possibility of a more prolonged anaesthesia than may be possible or desirable with nitrous oxide. (3) The use of an anaesthetic agent that does not demand any degree of anoxaemia and with which, if necessary, extra oxygen can be given. (4) Its use is free from any danger of explosion, and the bleeding is not likely to be so free, profuse and troublesome as it may be under cyclopropane.

From these theoretical advantages we are able to compile a list of indications for its use: (1) In rather more difficult or prolonged surgical procedures in the normal patient. Here the advantage gained is the prolongation and smoothness of the anaesthesia without subjecting the patient to any anoxia. (2) In normal surgical procedures on potentially difficult subjects for nitrous oxide anaesthesia. (a) The physically resistant type of patient—plethoric tough commando types and those who have acquired a certain tolerance to alcohol. Here the advantage gained is the rapid smooth induction of third stage anaesthesia. In nitrous oxide anaesthesia, the best that can be hoped for in the normal adult is first plane (Guedel) if enough oxygen be given. Resistant patients are likely to be partially asphyxiated in an attempt to reach surgical anaesthesia with nitrous oxide, and the end-result is likely to be a black patient in the stage of excitement, or even merely in the stage of analgesia and only too conscious of the extraction. (b) The mentally resistant patient: The patient who hates gas, who dislikes anything in front of his face and who gets a claustrophobic feeling under N_2O . Here the advantage is the rapid pleasant induction by the intravenous route. (c) The cardiac case, or the patient with pulmonary insufficiency. Here the advantage is that no degree of anoxaemia is necessary for perfect anaesthesia.

Contra-indication.—Pentothal should not be used in an attempt to do things in the dental chair which really ought to be done in the operating theatre with endotracheal anaesthesia, packing and suction.

Preparation of the patient.—The patient should have an empty stomach and an empty bladder. He should bring a friend to see him home afterwards.

Premedication.—Not usually possible and not necessary as a rule. Atropine grain 1/50 by mouth one hour before the appointment may be useful in helping to dry up secretions.

Position in the chair.—The patient should be sitting as upright as possible. This is important; in this position saliva and blood tend to stay in the mouth and are efficiently safeguarded by the oral sponge or pack from entering the pharynx. The chair should not be tilted backwards because in this position it is very easy for saliva or blood to trickle down past any oral pack and set up laryngeal spasm. The position should be comfortable and stable—legs uncrossed, knees bent, feet side by side, vertically under the knees. A pelvic strap is very useful—not for restraining the patient, which under pentothal anaesthesia should rarely be necessary, but to prevent the patient from slumping, when muscular relaxation occurs, out of the ideal position into which he has previously been put. Pentothal in the patient's bed for dental extractions should be avoided as a rule, but if it is done, the patient should always be given pre-operative atropine or scopolamine to dry up the saliva and only front teeth should be attempted in these circumstances, so that the dentist's manipulations will not be likely to cause obstruction of the airway and the oral pack and local swabbing and pressure will be effective in preventing blood running back to the throat.

Ideally, oral operations in the horizontal position should be made really safe by endotracheal intubation, pharyngeal packing and suction.

Technique of injection.—I use 5% or 2½% in the very old or debilitated—never a stronger solution than 5%. The dental prop is put in position. The arm is bared to above the elbow and should be well supported and stable—a large cushion supported on the patient's knees and the side of the chair provides a good method.

When the needle is in the vein, the first $\frac{1}{2}$ c.c. is injected very slowly. This is to make sure that the needle is intravenous and not intra-arterial. The patient will give ample warning of intra-arterial injection by complaining of an intense burning pain shooting down the arm.

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Posture.—The patient must sit well back in the chair, the head being in line with the body which should be as vertical as possible to the chair, the hands loosely clasped in the lap, and the feet and legs either drawn up or else on the floor or hanging towards the floor on either side of the foot-rest. Although a pelvic strap is used by many anaesthetists, I find that I can manage without this, and reserve it only for cases with a turbulent past history.

Procedure.—The anaesthetist should always inquire which teeth are to be extracted, whether any exceptional difficulty is likely to be encountered, and in which order the teeth are to be removed. As soon as the mouth prop has been inserted by the dental surgeon, the anaesthetist should commence the administration without delay.

The nose-piece is applied gradually, and a moderate and silent flow of pure nitrous oxide is presented. At the same time the anaesthetist talks quietly to his patient, encouraging him to relax all muscles and to breathe gently through the nose. The expiratory

valve is first fully open and the rebreathing bag shut off; then, after about half a dozen inhalations, the rebreathing bag is put into commission, the expiratory valve is gradually almost closed, and a careful watch is kept for evidence of surgical anaesthesia. Between the fourteenth and twentieth breath this will be recognized by various signs, such as the onset of slight cyanosis, twitchings of the palpebral muscles, absence of the conjunctival reflex, and automatic respiration. This last is the most dependable sign and may be accompanied by stertor.

When the first plane of the third stage of anaesthesia is reached, it is time to place an oral sponge or pack in position and to start dealing with the oxygen supply. These are the golden moments in which to secure a light and steady anaesthesia. If the patient is allowed to become more deeply anaesthetized, it is difficult to retrieve the position, because breathing will become deeper and quicker, cyanosis will increase, the muscles will become rigid, and jactitation caused by anoxia will ensue. If oxygen is added at this late stage, too much or too little is commonly given, resulting in an irregular and unsatisfactory administration. Thus, as soon as automatic respiration is observed, enough oxygen is added to relieve the growing cyanosis, and the extraction can be started.

The percentage of oxygen given at this stage will vary with the positive pressure at which the gases are delivered at any particular time, more oxygen being required at lower pressures and less at higher. In the average case, if the gases are being delivered at a pressure of between 5 and 10 mm.Hg, then 5% of O_2 gradually increased to 7% and then, if necessary, to 10%, will suffice.

The smooth regular narcosis resulting from a light surgical anaesthesia are much appreciated by both dental surgeon and patient; the surgeon has a relaxed, easily breathing patient on which to operate, unhampered by the excessive haemorrhage which accompanies cyanosis; the patient recovers promptly and comfortably from narcosis, without that exhaustion, faintness, sweating and nausea which so often follow an irregular administration in which there is a constant fluctuation between anoxia and over-oxygenation.

A good airway must at all times be maintained, and the anaesthetist must be ready to push the mandible forward from the angle of the jaw as occasion demands. The actual operation may interfere with the airway in two respects. First, in mandibular extractions the lower jaw may be pushed back, and if this cannot be remedied by forward pressure, the dental surgeon should be requested to pull the jaw forward, a service which most experienced operators will perform as a routine. Secondly, the nose-piece may be pushed upwards in the extraction of upper teeth so that the anterior nares are obstructed by the floor of the nose-piece. If this seems likely to occur, it is a simple matter to push the nose-piece down so that its lower edge lies midway between the anterior nares and the mucous membrane of the upper lip.

When the operation has been completed, the temptation to give a free supply of oxygen must be resisted unless this is definitely indicated. There is ample oxygen in the atmosphere, and plus quantities have an unfortunate tendency to produce a feeling of sickness. The patient's head and shoulders should be gently pushed forward so that any blood or saliva may trickle out of the mouth and not be swallowed.

During the recovery period silence should prevail, and any bright light should be diverted from the patient's face. After about three-quarters of a minute he is quietly asked to open his mouth so that the dental prop may be removed.

Nitrous oxide and oxygen narcosis often causes a partial amnesia, and the patient should not be stimulated into consciousness by any unnecessary noise, in fact the less said the better until he is obviously conscious and able to take an interest in his surroundings.

Mouth breathers.—Those cases where there is no actual nasal obstruction are best dealt with by using a mouth-piece of generous size and fitted with an expiratory valve. Truby's mouth attachment is the best and allows of a comfortable oral induction of anaesthesia. Once this has been established, most patients will unconsciously nose-breathe in a satisfactory manner; if not, an adequate throat pack plus a positive pressure of gases through the nose will ensure a smooth administration.

Patients with nasal obstruction may also be induced by the oral route, a small lubricated catheter being passed through one or other nares along the floor of the nose until its termination reaches the posterior border of the soft palate. The nose-piece is then reapplied and an ample supply of gas and oxygen is enabled to reach the nasopharynx and thus permit the administration to proceed normally. This technique was perfected by the late Dr. Silk in the Dental Department of Guy's Hospital as long as 1905.

To those *in statu pupillaris* or to the occasional dental anaesthetist a machine possessing the virtues of intermittent flow, physically correct calibration of oxygen percentage supply, known pressure of gaseous supply, graduated rebreathing, and an emergency oxygen supply are all of great assistance in attaining proficiency.

In many dental hospitals and in the dental clinics of general hospitals we commonly use the McKesson, the Magill, or the Walton No. 2, all of which possess these advantages. But in private practice, because of the weight and cumbersome nature of these, we generally use hybrid machines, of which the best known are the modifications made to Sir Frederick Hewitt's gas-oxygen stopcock by the late Dr. Bellamy Gardner and Professor Macintosh which, whilst easily portable, are of the continuous-flow type. Nevertheless, although entirely satisfactory in the hands of those who use them often, these machines are difficult to master by those who give only an occasional dental administration.

A portable apparatus is needed which comprises the virtues enumerated above, and these I think are incorporated in the "Portanaest", newly introduced by the British Oxygen Company. Thanks to the kindness of Mr. Charles King I have used this machine for a number of cases at Guy's Hospital and consider that an outfit of this kind will do much to improve the standard of administration by the occasional dental anaesthetist in private practice.

I will now deal briefly with four aspects of anaesthesia in the dental chair. First, the question of ever using nitrous oxide and air. I consider the true role of gas and air to be as an agent for the production of analgesia. For continuous nasal anaesthesia it cannot; for physical reasons, compare with gas and oxygen.

Secondly, remembering that all things are possible, it is possible to anaesthetize a co-operative child with nasal gas-oxygen for the multiple extraction of dentigerous teeth, especially if plus quantities of oxygen are used and the anaesthetist himself is an expert; but apart from these qualifications I submit that its use may be associated with struggling and terror to the child, and many a futile adolescence may conceivably be traced to this exposure to psychic trauma.

Surely the time has arrived for many of these children to be dealt with by the same technique as that adopted for the removal of tonsils and adenoids. A basal anaesthetic given in a nursing home or in the patient's own home, this being followed by an endotracheal administration of gas and oxygen with adequate packing off of the pharynx and the use of a suction apparatus, enables the surgeon to perform his work thoroughly and without haste, the child making a tranquil recovery without any psychological upset. I have myself given a number of these administrations and would strongly advocate a more general adoption of this technique.

Thirdly, in the case of anemic patients and the problem of adequate oxygen supply, it is possible to administer gas-oxygen, but its use cannot compare with that of cyclopropane plus oxygen or gas-oxygen, and this latter technique should always be employed where available.

Fourthly, it is possible to administer gas and oxygen to the difficult or resistant case by using premedication, positive pressure, sub-oxygenation, and the addition of lipid solvent adjuvants; but here again I would suggest that in these days the employment of intravenous barbiturates or cyclopropane is much to be preferred.

As to the safety of nasal gas-oxygen in the dental chair, Langton Hewer (1944) says that as a result of a questionnaire circularized in America, a total of 1,161,820 dental administrations of nitrous oxide revealed only two fatalities, a mortality rate of 0.00017%. Another series of 300,000 has been reported with no fatality. At Guy's Hospital the Dental School was opened in 1889 and since 1915 1,271,431 administrations have been recorded without any fatality. In my own practice I have no fatal cases to report.

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HEWER, C. LANGTON (1944) *Recent Advances in Anaesthesia and Analgesia*, p. 231, Fifth Edition, London.

Dr. John Gillies (Edinburgh) reported a series of over 800 cases in which cyclopropane had been administered to ambulatory dental patients. The agent was employed to supplement nitrous oxide and oxygen in cases where more than five minutes was required to complete the operation or where anaesthesia might only otherwise be obtained by excessive exclusion of oxygen. The advantages emphasized were: full oxygenation (especially necessary in very young or elderly subjects); quiet respiration with small tidal air volume which finds easy passage through the nostrils without the use of positive pressure; and very adequate anaesthesia and muscular relaxation with consequent avoidance of "smash and grab" surgery.

Dr. A. H. Galley (*Trichlorethylene*) said that he had now been using trilene in the dental chair for just over two and a half years. Since his preliminary report on the Single Dose Method (*Proc. R. Soc. Med.*, 1943, 36, 462) the investigation had been extended. First, trilene and air had been attempted by the nasal route, using a Marrett's apparatus and maintaining a slightly increased pressure by attaching a laboratory foot-pump: both the induction and recovery had been found to be rather slow when compared with nitrous oxide. Trilene was now administered as an adjuvant to nitrous oxide and oxygen—again by the nasal inhaler—and two machines had been employed: the "Walton" with trilene in the "ether" vaporizer, and the "McKesson" with trilene in a Rowbotham's chloroform bottle. Nearly 500 cases had now been anaesthetized in this manner with great success. Nasal trilene, nitrous oxide, and oxygen met the needs of the resistant patient without undue anoxia, induction was as rapid as with nitrous oxide; fluctuations in depth during maintenance could be minimized—an especial advantage when anaesthetizing children; greater percentages of oxygen could be used thus avoiding cyanosis and venous congestion; if the trilene were shut off some thirty seconds or so before the cessation of the administration recovery almost rivalled that of nitrous oxide. Owing to adequate oxygenation, the anemic, the "cardiac", and the chronic bronchitic types of patient could now be anaesthetized with much less danger. The complete lack of venous congestion greatly facilitated the operative procedure. Cardiac irregularities and the incidence of vomiting appeared to be no greater than with nitrous oxide alone. [A full report will shortly be published in the *Lancet*.]

Dr. Stephen Coffin mentioned that laryngeal spasm occurring during nasal nitrous oxide and oxygen anaesthesia could be detected in good time by observing a lateral curl of the tongue, forming a fore and aft trough, which is a very early and regular sign of this mishap. He said that two sets of props were of more use than two gags, which had been advocated by one speaker; he usually made changes by means of a second prop or by transferring the first, seldom using a Fergusson's gag. He preferred to stand at the side of the patient rather than behind, as advocated by other speakers, as control and assistance were easier so.

As to throat packs, untaped honeycomb sponges were the speaker's choice because, with proper care in watching the state of the pack, tapes were unnecessary and they could be a nuisance in the mouth.

He did not agree with telling the patient to breathe through the nose, which often produced exactly the opposite result; nasal breathing, in his experience, was the normal method of respiration in a comfortable induction and was best obtained by this means coupled with no advice on the subject.

For nasal dental anaesthesia Dr. Coffin always administered nitrous oxide oxygen (never air) and used an apparatus incorporating a Levy double bag and a Hewitt's mixing chamber. There were no valves. A comfortable nasal induction was obtained with a fast flow and the nose-piece off the face, and rebreathing or not during anaesthesia was controlled by the degree of apposition of the nose-piece.

Commenting on a statement made that intravenous anaesthesia in the dental chair was best undertaken with the patient sitting up to avoid laryngeal spasm from blood, &c., the speaker said that such a thing was unlikely in either a sitting or lying position (and in his experience had not occurred) with careful observation of the state of the pack. Dental anaesthesia in children was mentioned and Dr. Coffin said that children, when reasonably co-operative, were very easy to induce with nasal nitrous oxide and oxygen but much more difficult than adults during anaesthesia. A child should never be talked down to but treated as an equal: and with a proper approach, good technique and sufficient experience a child, in a large proportion of cases, could be anaesthetized without it realizing that it had had an anaesthetic.

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[January 23, 1945]

DISCUSSION ON THE DEVELOPMENT OF HEALTH IN ADOLESCENTS

Brigadier Frank Howitt: It is a curious thing that the medical profession, whose recent tendency it has been to specialize and departmentalize more and more, should have paid so little attention to the problem of adolescence. New departments have been built up, specializing on the one hand in system or disease groups such as cardiology or endocrinology, and on the other hand in age-groups such as pediatrics and antenatal care. One even hears that there is a movement afoot to promote a section of geriatrics, the science of the ageing process! Diseases are being segregated, and diplomas are springing up like mushrooms in the field. Yet adolescence, that most important period in life, during which a man's future is made or marred, has never received sufficient attention from the medical profession.

I propose to divide the subject under three headings: The position as it existed before the war; the wartime impetus; and the possibilities with regard to the future.

THE PRE-WAR POSITION

There are many reasons why the achievement and maintenance of health in adolescence made no popular appeal before the war.

In the first place there was the political factor. Anyone, outside the fighting Services, who came forward with such a demand in peacetime would have laid himself open to the charge of militarism. You could initiate dental and maternity clinics, institutes for the blind and deaf, homes for epileptics and sufferers from cancer, and money would very properly flow into your subscription lists. You could invoke Government aid. But suggest the need for national physical fitness, and you were regarded at once with the gravest suspicion. And there were reasons for this—the precepts of Germany, Italy and Japan. Neither had the adolescent a political foster parent. He lived in the no-man's land between the realm of the Board of Education and that of the Ministry of Labour.

Secondly, there was the economic factor. The increasingly long hours of work demanded by the progressive but predatory incursions of education and of industry into the life of adolescents left them with neither the time nor the inclination for self-improvement. Hence came the growing tendency of the young worker to take his exercise vicariously at the ringside, and as a natural corollary, the appearance and importance of the professional. With the advent of the expert, came a disinclination on the part of the less-gifted or inferior exponent to make any competitive effort at all. So there developed a tendency on the part of the mass to give up the unequal struggle and to spend their leisure hours in watching contests rather than in taking part in them. Thus was produced a nation of onlookers. Neither in such circumstances was this to be wondered at, for as civilization progresses, the demands made on mental capacity increase, whereas physical attributes are relegated to a position of secondary importance. A man's output is limited to a certain number of ergs of energy, and he cannot be blamed for regarding himself from the economic viewpoint.

Thirdly, there was no motive through which to make an appeal to a freedom-loving country such as ours. For without a motive you will not, in peacetime, obtain either from youth itself, or from the parents of youth, any general consent or enthusiasm for physical improvement.

Fourthly, the development of health in youth is a social issue in which there must be co-ordination between medical science in all its aspects, and all non-medical services interested in physical education, using that term in its widest sense, and not in the restricted form by which it is commonly understood, particularly by the medical profession.

Before the war, with the exception of certain recognized professional associations, interested mainly in educational work, this duty—as far as the masses were concerned—

was undertaken by isolated organizations which struggled in a parochial way to promote physical fitness.

Medicine placed too much emphasis on the study of disease, and too little on that of health. It searched for the cause of symptoms, too often within the body, and too seldom in extraneous causal factors.

State education placed too great an emphasis upon academic, and too little on physical improvement. It commonly confined its activities to the wall surrounding the school-yard, and to the hours laid down in the curriculum. It relinquished its burden at the school-leaving age, disregarding the fact that the most important years of life lie immediately ahead.

Industry, with the exception of certain large and enlightened firms failed to appreciate that the optimum health of its employees, particularly its juvenile employees, is an asset; and that substandard health, which is commonly the harbinger of serious disease and disability, yields a poor economic return. It failed to seek advice with regard to the physical welfare of its operatives, and on problems conducive to the conservation of energy.

Organizers of sport and athletics were prone to cater for the few which excelled rather than for the mass which did not, disregarding the fact that the national need for the physical improvement of the substandard to normality is far greater than the need for the promotion of the normal, in certain selected instances, to the super-standard of the professional.

It is to the credit of the Army that there were in existence in these pre-war days two Army Centres which catered for young recruits who did not attain the high statutory physical requirements of the Service at that time. At these, excellent results were obtained, but they had to be closed on the outbreak of war, owing to the need for barrack accommodation.

THE WARTIME IMPETUS

The first of the present Army Physical Development Centres was opened in September 1941. Since that time, others have been added. Their object is twofold. First, to hold courses for young recruits of poor physique due to underdevelopment and mal-nutrition, and for those with abnormalities and early local skeletal defects, due to postural, occupational and environmental causes; and secondly for soldiers in Field Force Units who have broken down on poor locomotor or other grounds. It will be seen, therefore, that the function of these Centres is both preventive and corrective.

It has been the good fortune of Army Physical Medicine—and here it may be noted that Army Physical Medicine regards itself as part of General Medicine, and not as a therapeutic speciality—to be entrusted with the selection of cases for reference to the Centres, for their medical control at the Centres and for their final assessment.

Selection is of the utmost importance as it is necessary that only cases likely to show substantial improvement should be sent, and those associated with rigid deformity should not be included.

Neither fixed ideas nor hide-bound convention have influenced the organization or administration of these Centres. Rather have they progressed and developed with their expansion. A catholic view of physical education has been taken, and an attempt has been made to attack the problem from all aspects. The regime has been built up on teamwork in which the physical, psychological, educational, social and nutritional aspects have all been borne in mind.

I will take these factors separately.

Physical training instructors of the Army Physical Training Corps have been carefully selected for their aptitude in dealing with this type of case, and have been specially instructed in the elements of physiology, the principles of functional anatomy, and the application of active exercises in the treatment of deviations from the normal. The system evolved is based on the principle of leadership, combined to produce a balanced combination of strength, agility and alertness. It is insisted that the mind should control intelligently the development of the body, recognizing that on the nature of this control, depends the quality of character. A vital atmosphere is thus created, so that thought and enthusiasm regulate action. Training by interest is made the key-note of instruction. Thus a system of preventive and corrective treatment has been built up to meet the specific demands of the Army. The trainees are grouped into classes according to their disabilities and the exercises progress in a graduated sequence of energy expenditure. The aim is to produce a correct habit of posture, of locomotion and of performing physical tasks, and this can only be attained by constant repetition. Supervised progression is fundamental to all physical training, and the final demands are reached by a steady increase in load, frequency and distance. The necessary mental stimulus is provided by the inclusion of games of a quickening and co-ordinating char-

acter. Particular attention is paid to the prevention of fatigue, both physical and mental. In preparing the daily programme of each group, the periods are arranged so that the more strenuous sessions alternate with those of a more recreational nature. There is a break in the mid-morning and trainees again relax on their beds for half an hour after the midday meal. Attention is given to the proper use of leisure when the day's work is done. Experience in athletic training and knowledge of physiological reactions are necessary in order to prevent staleness and boredom.

Individual treatment is available for those requiring it. Physiotherapy is undertaken by qualified members of the Chartered Society. Particular attention is paid to skin stimulation. There is a boot inspection during the first week, when all misfitting and badly worn boots are replaced, and special cases are referred to the cobbler with prescriptions for temporary alteration. The chiropodist has a most important function to fulfil. In addition to treating corns, blisters, ingrowing toe-nails and other abnormalities, he gives instruction in the maintenance of foot hygiene. Every adolescent is given a thorough dental overhaul; in the largest of these Centres there are eight dental surgeons working full time. There is a resident messing officer whose duty it is to supervise the cooking, and the manner in which meals are served, as the psychological effect of this is considerable. For obvious military reasons, however, it is not possible to make the qualitative alterations to the diet which would be desirable in this type of case.

The Army Education Corps renders valuable assistance by way of physical relaxation and mental stimulation. The educational subjects taught, whilst retaining a popular aspect, are chosen with a view to maintaining a continuous service on a man's behalf as a soldier.

Routine medical examinations take place at the beginning, middle and end of every course, but progress is supervised throughout, and any special treatment considered necessary in individual cases is prescribed accordingly. In assessing the final medical category, the results of performance throughout the course are given great consideration. Although certain tests, such as the Harvard pack test may give a reasonable index of the actual performance-ability at the time of the test, it is unfortunate that no anatomical or physiological test capable of measuring potential physical performance has yet been devised. The exercise tolerance test, the vital capacity estimation and pedograph measurements are equally at the mercy of the enthusiast, the malingerer and the moron.

Many interesting facts have emerged as the result of more than three years' experience of Physical Development Centres. The type of case most likely to respond to training has been established. The relative value of different kinds of exercises and treatments has been assessed. The true value of various tests of physical efficiency has been examined, and their sphere determined. It has been proved also that improvement is effected in the mental as well as the physical alertness of the trainees.

The factors underlying the various clinical conditions have been occupying the attention of Physical Medicine since the inception of these depots. Recently the services of the Directorate of Army Medical Research and Statistics have been enlisted with the object of correlating by laboratory and field research, deductions made on a purely clinical basis. The Army has to take a realistic attitude, and the value of research is strictly assessed in relation to the extent to which it furthers the war effort. Certain investigations are in process of determination, including an attempt to establish criteria of normality, an anthropometric survey of physique in relation to performance, and an investigation into the social, occupational and environmental aetiology of poor physique. The incidence and significance of march fracture, and of spinal epiphysitis are being determined. The hæmoglobin levels of substandard recruits are being assessed, and related to the clinical condition, including dental survey and chest radiography. In this connexion, the results seem to suggest that, whereas the hæmoglobin levels may be increased, as the result of training, in those cases in which they were originally low, they may be correspondingly decreased in those cases in which they were originally high. This suggests that there is an optimum hæmoglobin level associated with physical fitness.

It should be mentioned that a Centre has now been established for the physical improvement of substandard recruits of the A.T.S. The objects to be obtained differ, of course, from those demanded of the men, and the methods of obtaining them require a different approach and technique. It is, for instance, at no time necessary to develop a high degree of strength, as no Auxiliary is expected to lift a weight of more than 40 lb. On the other hand, the duties of this service—cooks, orderlies, &c.—often entail long hours of standing on concrete floors, and in trying atmospheres. This is but another example of the necessity for purposefulness in all physical training. The Auxiliary is fully aware that she is not being prepared to face unknown danger and

hardship. But I would like to pay my tribute—as a mere male, and a bachelor at that—to the willingness with which these girls apply themselves to the routine of training, and to their appreciation of the feeling of well-being which results from physical fitness.

THE POSSIBILITIES OF THE FUTURE

It is good to note that the Ministry of Health in conjunction with those of Labour and Education is considering the initiation of a Centre for civilian substandard youths. There are, of course, many difficulties which such an enterprise would have to face. Chief amongst these are money and compulsion, which translated into peacetime terminology, means persuasion; and persuasion is dependent upon motive.

With regard to money, it is admitted that to equip and administer a Centre of this nature would involve considerable expense both in capital and maintenance, for it would be fatal to embark upon such a scheme, unless it were done well.

On the question of motive, it must be realized that in this competitive world—democracy or no democracy—everyone must fend for himself. The appeal must therefore be pragmatic and practical, even selfish, and based on the lure of heightened individual efficiency, with resultant self-advancement and an increased earning capacity and prestige. There is in the body of British youth, a new awakening to a sense of personal interest and responsibility. The substandard youth takes great interest in the correction he observes in his defects. He comes to appreciate the value of health; not only in relation to capacity for enjoyment, but also as a means of increased economic opportunity.

A Civilian Centre would involve certain differences in technique from the Army scheme. The age-group would, preferably, be somewhat lower. The educational aspect would become relatively more important, and would assume a somewhat different character. In place of subjects such as military geography and map-reading, important to the soldier, the civilian youth would need to learn about civic responsibilities and local affairs. The final recommendations as to placement in industry would require a method of selection, designed to meet the requirements of the various civil trades. But the procedure, adopted in Army practice, which has emphasized the importance, not merely of finding a job for a man, but of finding the right job for him, should be followed. He must be placed in an occupation which fully exercises all his available faculties, and not in one which is within the easy compass of his competence. It must also be remembered that the more favoured members of the community are able, at an early age, to make up their minds as to which trade or profession they wish to adopt and have the opportunity either of pursuing it, or of taking up another before it is too late. The less fortunate, because of social or environmental circumstances, or because of a short-term policy of economic return, are often lured into a vocation entirely unsuitable. It is surprising, also, how inept is even the normal but uninstructed individual in the performance of even the simplest tasks, such as digging, lifting, jumping and climbing. When dealing with the substandard, correction of faulty technique may not only prevent further disability, but may be productive of considerable economy of energy. The training at such a Centre must, therefore, be purposeful in character, and designed in accordance with individual potential capacity, both mental and physical. It must not be haphazard or stereotyped. When the final assessment has been reached vocational guidance should be available, based on the advice both of doctors with experience in this field, and of experts conversant with the varying demands of the different branches of industry. The final boarding would therefore be a most important sequel to the purposeful training at such a Centre.

In hospitals there should be a preventive as well as a curative department. To this preventive clinic should be referred all cases—so common in adolescence of substandard health, such as fatigue states, anæmias, recurrent infections and early structural deviations—conditions which are sometimes contemptuously and foolishly referred to as minor medicine. Very often such conditions are observed, parenthetically, in the course of the routine clinical examination of an out-patient presenting himself for some immediate and entirely separate cause. These are the conditions, which, taken early, are often entirely correctible, but which, untreated, may progress insidiously until serious symptoms arise. In such a health department there should be free and intimate collaboration between the various medical and surgical departments and specialities, and between those doctors and the various medical auxiliaries, including lady almoners, physiotherapists, physical educationists, dietitians and chiropodists, and between these auxiliaries themselves.

The medical student should be taught how to detect disease and disability in its early and preventive stages, and be instructed in the special problems of school and industrial medical officers. The hospital should form a closer liaison with

those services and with any recognized physical development or other youth Centres which may eventuate.

Major-General Sir Guy de C. Glover: Although various officers had been thinking about physical development in the Army some time before, the first instance was when Major Wand-Tetley, in command of the Wiltshire Depot, asked permission to try and develop about 20 recruits who were below Army standard. This was approved and the course was a success.

A Development Centre was then set up at Aldershot and afterwards moved to Canterbury, and an additional one set up at Scarborough. The Army was really driven to this procedure owing to the shortage of recruits for the Regular Army and the large number of potential recruits who were rejected as they were not up to medical standard. At times this ran into 60% of the applicants.

These units were military units in every sense with a combatant officer in command and besides dealing with the physical infirmities of the men, dealt with the question of *esprit de corps* and well-being. The units turned into first-class military units and the majority of the men into good soldiers. When the Militia scheme started in 1939 they had to give up their accommodation, but up to that time, out of about 2,700 who had been through the units, 2,000 had been upgraded and accepted as recruits up to the Army standard.

In 1941 it was again possible to deal with this problem and a Physical Development Centre was started at Kingston-on-Thames. Now there are three with a capacity for 2,500 men. The results obtained have been most remarkable and of the greatest benefit to the Army and to the men concerned. Two types of men gain value from the units: those underdeveloped or not up to medical standard on enlistment, and those who have broken down in some way during their military training. The latter category are chiefly men with bad feet. There is no doubt that a man's mental outlook is improved as well as his physical condition because from selection testing it has been proved that at least 10% of the men are able to raise their intelligence standard from below the normal to above.

Of the 26,733 who have been through the units about 20,086 have been medically upgraded. They are also in most cases far better soldiers and from the educational training they get at the units, they are better educated men when they leave.

The Physical Development Centres must not be confused with Convalescent Depots which are purely medical units dealing with men convalescent from sickness or wounds, although a fairly similar system of training is carried on at Convalescent Depots.

There is no doubt that these units are very valuable and the Army proposes to carry them on. They would be, I feel sure, of the greatest value in civil life but it is realized that the difficulty of organizing and running them on a civilian basis is far greater than in the Army. In any case the Army will be in a position after Release commences to provide civil authorities with a number of highly-skilled instructors who have worked at these units and I hope that their valuable knowledge will not be wasted to the community.

These Physical Development Units have been of the greatest assistance to the Army and to the men who have been through them and the Army means to go on with them.

Sir Adolphe Abrahams: I propose to confine myself to one aspect of adolescent associations: the influence of competitive exercise particularly in respect to the claim that serious injury to the heart may occur, a charge repeated from time to time notwithstanding the pronouncement of School Medical Officers whose Association after due investigation came to the conclusion that no such evidence is forthcoming.

It is confidently maintained by cardiologists that the reserve of a healthy heart is so considerable that no effort however great can produce any harmful effect. When the call is excessive other less important factors fail. The heart represents the central fortress of the organism, the defending position and outposts being provided by the nervous system and its servants. When alleged cases of heart strain are examined, it is found that some are examples of long-standing lesions which having given rise to no symptoms have been unrecognized until the breakdown; some are merely instances of innocent natural peculiarities mistaken for pathological conditions; and some, the majority, are the symptoms of nervous instability with special reference to the vasomotor system. The frequently observed failure of schoolboy athletic prodigies to develop in accordance with their early promise is regarded as evidence in support of the idea of strain or premature exhaustion—the so-called "burnt-out" athlete. But athleticism like growth and development is individual. Rarely, the boy who shows a high promise proceeds regularly and uninterruptedly to a supreme level in early adult life. Temporary decline with subsequent rises and falls generally occur; and discouragement when the period of declivity is encountered often leads to a fatalistic acceptance of permanent deterioration.

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It is confidently maintained by cardiologists that the reserve of a healthy heart is so considerable that no effort however great can produce any harmful effect. When the call is excessive other less important factors fail. The heart represents the central fortress of the organism, the defending position and outposts being provided by the nervous system and its servants. When alleged cases of heart strain are examined, it is found that some are examples of long-standing lesions which having given rise to no symptoms have been unrecognized until the breakdown; some are merely instances of innocent natural peculiarities mistaken for pathological conditions; and some, the majority, are the symptoms of nervous instability with special reference to the vasomotor system. The frequently observed failure of schoolboy athletic prodigies to develop in accordance with their early promise is regarded as evidence in support of the idea of strain or premature exhaustion—the so-called “burnt-out” athlete. But athleticism like growth and development is individual. Rarely, the boy who shows a high promise proceeds regularly and uninterruptedly to a supreme level in early adult life. Temporary decline with subsequent rises and falls generally occur; and discouragement when the period of declivity is encountered often leads to a fatalistic acceptance of permanent deterioration.

Even if satisfactory argument has been advanced in controversion of the alleged dangers of violent effort what is to be said in its favour? It is a form of education to learn the resources of strength and endurance of one's body with repercussions upon the more important activities of life especially when the character is at its most malleable stage, the time when violent exercise is psychologically acceptable and physiologically possible. It is regretted that too much adulation is accorded to the great athlete who acquires a wrong sense of values, and one may be disposed to submit that the chief danger to the adolescent is not an enlarged heart but an enlarged head.

In regard to girls and young women, with appropriate modifications the same physiological and psychological details must be equally pertinent and pressing. It may smack of Victorian narrow-mindedness and prejudice to display solicitude for the preservation of those qualities traditionally associated with femininity and the avoidance of the danger of over-development of certain masculine traits by indulgence in severe competition, as well as the disadvantage of diverting energy from channels for which it is particularly required in preparation to bear the burdens of womanhood and possible motherhood. Some gynaecologists, despite special investigations which would appear to prove the contrary, remain unconvinced that muscular development does not prejudice normal pregnancy and parturition.

The nervous side deserves paramount consideration. Highly competitive efforts such as First Class Lawn Tennis Tournaments in which the leading players attain a wide publicity create a wrong sense of values and produce an anxiety state and general ill-health which are not so much the direct consequences of exertion as of the concomitant circumstances.

Dr. G. E. Friend: The development of health in adolescence depends upon: (a) The provision of an adequate and well-balanced diet; (b) the provision of adequate sleep and rest; (c) a properly balanced physical development, which in turn depends on a correct ratio between games, physical training, and education in personal and environmental hygiene; (d) avoidance of over-fatigue, mental as well as physical.

The chief function of a school medical officer is preventive rather than curative or clinical.

This is not to decry the clinical side of school medicine. On the contrary the school M.O. needs to have a sound working knowledge of general medicine, minor surgery, ear, nose and throat, skin and infectious diseases. He requires the same psychological background as the older family physician, and a working knowledge of both public health and hospital administration. In the private and public boarding school, at any rate, he should be given a reasonably free hand, and should be directly responsible to the governing body and chairman of the school committee. He must have the confidence of the headmaster, and be in close liaison with the games committee, the director of physical education, of swimming and other activities, especially the Junior Training Corps, Air Training Corps, Scouts or other like organizations. At the same time he should have the confidence of the boys and make them realize that they can come to him for advice or help at any time, with the certainty that, within the limits of school law, their confidence will be respected.

The not uncommon idea that schoolboys are liable to regard the M.O. as only of use in sickness (and so foster a sickness-complex) is wrong and is much to be deprecated. He can do much to lay emphasis on health rather than on the cure of disease, by his interest in games, Physical Training, Swimming, J.T.C., A.T.C., Scouts, &c., by talks both official and informal to boy-groups of all ages in the school, and by being readily accessible for advice and help on many subjects outside his own particular line.

Motive.—The Greek ideal of perfect physical development and fitness for its own sake. According to the school code a boy may be keen on the J.T.C. if in the Army class, without stigma, as this is considered selfish and therefore right; though, in fact, boys are intensely patriotic but hate to admit it. J.T.C. and A.T.C. are unpopular with the majority because they are compulsory and take time from games. A.T.C. is less unpopular as there is less drill.

Games and sports on a house competitive basis are definitely character forming—you play for the side and not for yourself—J.T.C., A.T.C., Sea-Scouts, &c., are not so good as at present organized. They would be better, and probably produce better material, if amalgamated with a common basic all-round training, more on Scout lines than as now established—less marching and forming threes or fours; more P.T., shooting, and real week-end camping where the boys do their own cooking and tent-pitching, first aid and hygiene; attend to and learn about machines and engines, field craft, map reading, methods of signalling, wood and metal work.

Section of Urology

President—F. MCG. LOUGHNANE, F.R.C.S.

[November 23, 1944]

The following specimens were shown:

- MR. E. W. RICHES: Seminoma of Undescended Testis.
MR. R. H. O. B. ROBINSON: (1) Teratoma of Undescended Testis. (2) Calculous Pyonephrosis.
MR. TERENCE MILLIN: Bone Formation in Kidney Following Injury.
MR. J. GABE: (1) Calculous Hydronephrosis Following Ruptured Kidney. (2) Embryoma of Kidney.
MR. T. L. CHAPMAN: (1) Papillary Carcinoma of Renal Pelvis (Left Side), Renal Calculi (Right Side) and Papillomata of Bladder. (2) Calcification in Scrotal Lipoma.
MR. A. WILFRID ADAMS: Tuberculous Bladder and Internal Genitals from a Boy of 10 Years.
MR. HUGH DONOVAN: Normal Intravenous Pyelo-ureterograms in Spinal Cord Injuries.
MR. HENRY K. VERNON: (1) Ectopic Vaginal Ureter Treated by Heminephrectomy. (2) Hydrocalicosis.
MR. HOWARD G. HANLEY: (1) Bilateral Megalo-ureter. (2) Ureteric Transplantation for Multiple Pelvic Injuries [Patient shown].

[January 25, 1945]

The Diagnosis and Treatment of Male Infertility.

By KENNETH M. WALKER, F.R.C.S.

CHILDLESSNESS in marriage is far more frequently due to varying degrees of subfertility in one or in both of the partners than to complete sterility. It is therefore subfertility which is of greatest interest to urologists. Unfortunately no reliable statistics are available by which we can assess the incidence of subfertility in this country, or can apportion the blame for childlessness between the two partners in marriage. Percentages ranging from 10 to 15 have been given for the incidence of marriages throughout the country which are involuntarily sterile. Permanent childlessness is rarely deliberate, although many couples by the use of contraceptives may defer the arrival of the first child. This conclusion is based not only on medical experience, but on special investigations which have been made by a group of researchers with whom I have long been associated.¹ Our investigations have also shown that the contraceptive methods commonly used by the working classes are notoriously unreliable, and that they mask a condition of lower fecundity in at least a third of the people using them. There can be little doubt therefore that subfertility is a common condition in this country. As it is only comparatively recently that investigations have been undertaken, it is impossible to compare present with past conditions and to assert that subfertility is on the increase but it is not unlikely that this is the case.

Responsibility of husband.—In the absence of reliable statistics it is impossible to say how frequently the husband is responsible for childlessness in marriage, but we will probably not be far wrong if we say that in one-fifth of all barren unions he is so infertile as to preclude for all practical purposes the likelihood of his wife's conceiving and that in about two-thirds of them his fertility is so low as to render conception relatively improbable. It is extremely important to remember that in the great majority of cases there are no outward signs to suggest that these husbands are infertile, and it is only after their semen has been submitted to examination that this condition is discovered.

¹ The observations I have given here are not mine alone but those obtained from the combined work of Dr. Lane Roberts, Dr. M. Barton, Dr. B. P. Wiesner and myself.

The prevalence of subfertility is also revealed by the fact that a great many of those who offer themselves as donors of semen for artificial insemination are found to be unsuitable for this purpose.

Veneral disease, on which so much stress has been laid in the past, is of comparatively little importance as a cause of infertility. Nothing will be found to be wrong with the genital tract in most cases. Since, however, the germinal cells are sensitive to pathological changes in other parts of the body, and particularly to infections, the clinical examination must not be confined to the genital organs, but must embrace the whole of the body. Emphasis has been placed by some American writers on the importance of endocrine disturbances as a cause of male infertility, but in my experience, if this be so, these disturbances are not such as to be revealed by any clinical examination. In a few cases hypopituitarism associated with hypogonadism will be found, but they are exceptional.

SEXUALITY

Since conception depends on the presence of healthy spermatozoa in the female passages at the time of ovulation, the clinical examination should include an inquiry as to the frequency and effectiveness of sexual intercourse. Other things being the same, conception will be almost twice as likely when intercourse takes place weekly than when it occurs only once a fortnight. Nor must it be presumed that intercourse is satisfactory. Strange as it may seem, there are cases in which the husband fails to complete the sexual act and never ejaculates, a deficiency which is sometimes only revealed when he is asked to produce a specimen of semen for analysis. Such cases are invariably psychological in origin, occurring in men of weak or inhibited sexuality. Not infrequently the retained sexual secretions are ejaculated during the hours of sleep following the incomplete coitus. The common marriage difficulty of premature ejaculation must also be considered. This does not preclude conception, but if ejaculation always occurs in the vulvar region, it renders it less probable.

SEMEN ANALYSIS

Semen analysis has developed so rapidly during the last few years that it is now a work that can only be undertaken by experts. Semen must not be collected for examination by the use of a condom but should be obtained either by withdrawal, or by masturbation.

Absence of motility.—During recent years I have seen quite a number of men who have been said to be suffering from necrozoospermia—a comparatively rare condition—solely because the motility of their spermatozoa had been arrested by traces of chemicals in the condom employed. Sometimes arrested motility is not due to rubber but to the patient having warmed up the semen, an action which causes excessive movement followed by exhaustion. Another point I should like to make is that the spermatozoon count is of far less importance than some American authorities would have us believe. It is nonsense to suggest that a man with under sixty million per c.c. is to all intents and purposes sterile.

Number of spermatozoa.—Of far greater importance than the number is the quality of the spermatozoa present, and a high percentage of abnormal forms is of bad significance. Other points which have to be taken into consideration are the volume of the semen, its viscosity, the rate of liquefaction, the tendency, or not, for the spermatozoa to agglutinate spontaneously, their motility and viability and the presence in the specimen of organisms not due to artificial contamination.

POSTCOITAL TESTS

The behaviour of the semen *in vitro* is one thing and its behaviour when mixed with the female secretions is another. The healthy cervical secretion is a highly favourable medium for the survival of spermatozoa and they may survive at least three times as long in cervical mucus as they do in their own seminal fluid. The carrying out of a postcoital test on the wife is therefore often a very important item in the investigation of childlessness, an item which is too often neglected. This is often referred to as a Huhner's test, but as it was first advocated by that astute gynaecologist, Sims, it should really bear his name. By means of it we can discover whether the invasion of the cervical plug with spermatozoa—a *sine qua non* for conception—actually occurs. Lack of cervical insemination is a frequent cause of sterility which is not discovered by any other means. It may be due either to faults in the spermatozoa (poor motility and viability) or else to changes in the cervical plug. The more successful the invasion, the more likely conception is to take place, but conception sometimes follows even when

only a comparatively few motile spermatozoa are found within the cervix. Receptivity of the cervix is apparently at its height during the ovulatory phase, but Drs. Barton and Wiesner state that they "cannot confirm the claim that the cervix will never admit spermatozoa in the pre-ovulatory or luteal phase of the cycle" (*Lancet*, 1944 (ii), 563).

TESTICULAR BIOPSY

Microscopic examination of the seminiferous tubules is a valuable method of investigation and fortunately it imposes but little hardship on the patient. All that need be done is to expose the testis through a half-inch scrotal incision, puncture the tunica albuginea with a sharp-pointed tenotome and remove the button of testicular tissue which presents itself with iridectomy scissors. As it is difficult to render the puncture of the testis painless by a local anæsthetic, I now prefer doing this under pentothal. Biopsy is of great assistance in diagnosis, for it allows us to correlate the state of the semen with that of the testis. It also gives us valuable information on the subject of prognosis, and tells us whether it is worth while attempting to stimulate activity in the tubules by any form of hormone therapy. One interesting observation derived from testicular biopsy is that wide variations are often to be found in different areas of the testis, at some points the tubules being completely degenerated, and at other points active even up to the phase of spermatogenesis. Testicular biopsy should also be used in all those cases in which doubt exists as to whether the absence of spermatozoa in the semen is due to aspermatogenesis, or to occlusion of the ducts. The method of differential diagnosis advocated by Huhner, namely, testicular puncture with examination of the aspirated fluid, is in my experience, entirely unreliable.

TREATMENT

Subfertility is compatible with excellent general health, but any defects in health should not be neglected when subfertility is discovered. All forms of chronic infection whether in the genital tract or elsewhere in the body must be eliminated if possible. Recently I became involved in a correspondence because I had stated that the sulphonamides might have an adverse effect on the germinal epithelium. Animal experiments suggest that this is the case, but sometimes the advantages to be gained by using these drugs for the elimination of a persistent infection outweigh the disadvantages of their possible action on the tubules. Fortunately the latter appears to be of a temporary nature. When bacteria are found in the semen, they may sometimes be got rid of by the use of an old remedy brought to my notice by Dr. Wiesner, namely, garlic, and there are several babies in this world at the present moment who owe their existence to this odoriferous and pungent herb.

Garlic may be used either as a fresh infusion of the herb made by the patient, or as an extract. If it is to be efficacious, the latter must contain the alcohol and acetone soluble fraction. The activity of the extract should also be tested bacteriologically. In our own work, carried out in conjunction with Dr. H. Coke, the extracts were tested regularly in dilution series against strains of staphylococci. But it is also necessary that they should have a bactericidal action on Gram-negative organisms. American writers have recently carried the work of extraction to a further stage, but we still prefer the use of extracts freshly made by the patient.

As failure to conceive may be due to infrequent or incomplete intercourse, treatment may resolve itself into dealing with the husband's sexual difficulties. Some of these weakly sexed husbands comfort themselves with the thought that abstinence enriches the semen. Recent work at Cambridge shows that the reverse is the case and that reasonably frequent intercourse improves its quality. Of course intercourse during the ovulatory phase in the female is of particular importance.

I do not know whether it is only because I personally see so many of these cases but I have been given the impression that sexual difficulties are on the increase. It would almost seem that in civilized man certain instinctive capacities, and amongst them those connected with breeding, are weakening. I remember how struck I was when shooting in East Africa many years ago by the superiority of sight, smell and hearing in more primitive people. May it not also be that our potency and our fertility are declining, and that there are bigger factors in this problem of infertility yet to be discovered?

HORMONE TREATMENT

Two hormones are of value in the treatment of male infertility, testosterone and anterior pituitary and related hormones. The former, though in certain conditions capable of acting on the testis, acts chiefly on the accessory sexual glands and particularly on the epididymis. This organ is far from being only a convoluted duct with no

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[February 22, 1945]

DISCUSSION ON THE RADIOTHERAPY OF TUMOURS OF THE KIDNEY AND BLADDER.

Air Commodore Stanford Cade: *Tumours of the kidney.*—The key to a rational radiotherapeutic treatment of renal tumours is a consideration of their natural history. A study of their morbid anatomy, histological features and clinical course shows that these tumours fall into three main groups, each a distinct clinical entity and of different histogenesis. These three groups originate from the three main elements which participate in the formation of the kidney. From the epithelium of the renal parenchyma originates the adenocarcinoma; from the mesodermal tissue and structures derived from it the adenosarcoma; and the transitional epithelium of the lining of the renal pelvis and calices gives origin to the papillary or epidermoid carcinoma. These terms, adenocarcinoma, adenosarcoma and epidermoid carcinoma are preferable to the better known, but inaccurate and now meaningless, terms hypernephroma, Grawitz's tumour, Wilms' tumour, nephroma, embryoma, renal blastoma, teratoma, &c. Of the many features of these tumours, I shall mention only those which influence the choice of treatment.

The course of the disease.—*Adenocarcinoma of the kidney*, both from its structure and its behaviour, is a slow-growing tumour—it is clinically silent as long as its spread is still intrarenal and it asserts itself only a little when direct invasion of the perirenal tissues or of the epithelial lining occurs. The period of relative silence is followed, after a variable interval, by rapid and widespread effects of an explosive character, which manifest themselves by the multiplicity and wide distribution of metastases. The occasional solitary metastasis only emphasizes the devastating nature of the tumour in the majority of cases. This sequence of events is inevitable if the structure of the tumour is considered, namely the sinusoidal character of the blood-spaces within the tumour, the thin-walled vessels with a single layer of endothelial cells separating the systemic blood-stream from the neoplastic cells. The burden of the dissemination falls on the skeleton and the lungs; the normal structure of these two tissues shapes the destiny of these deposits, thus the bones decalcify as a result of the vascularity of the tumours; hence the main characteristic of the skeletal metastasis is its extreme osteolytic power, which literally wipes out the bony trabeculae of the host. Similarly, in the lungs the metastases are spherical from rapid centrifugal growth, multiple and variable in size, as they arise in successive generations or crops. It is essentially a tumour of the fifth and sixth decades of life and occurs in otherwise normal kidneys. I have yet to meet an adenocarcinoma of the kidney in an organ the seat of chronic nephritis, in association with persistent infection, gross stone formation or hydronephrosis.

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Epithelioma of the renal pelvis.—These tumours are rare—about 7 to 10% of renal tumours. The incidence in men is three times as great as in women. There are two types, the papillary, which is common, and the non-papillary, which is extremely rare.

TABLE I.—CONTRAST BETWEEN PAPILLARY AND NON-PAPILLARY NEOPLASMS OF THE RENAL PELVIS.

	Papillary	Non-papillary
Predisposing cause	None	Leukoplakia, stone
Histology	Stratified transitional-cell carcinoma	Squamous-cell carcinoma
Incidence	80%	20%
Gross morbid anatomy	Papillary	Ulcerative, infiltrating
Mode of spread	Surface implantation, metastasis	Invasion of wall of pelvis, kidney and perirenal tissue
Chief symptom	Hæmaturia	Pain
Prognosis	Relatively good	Extremely grave

Principles underlying treatment.—The main treatment of malignant growths of the kidney is surgical—nephrectomy or nephro-ureterectomy. It may be asked, therefore, what place, if any, does radiotherapy hold in the therapeutics of this malady. The answer should be looked for in the critical study of (a) the prognosis after operation, (b) the effects of radiation on the tumours, (c) in the treatment of recurrences and metastases.

other function than that of storing spermatozoa. By its secretions the epididymis assists in the bringing of spermatozoa to maturity and a deficiency in its function is a cause of asthenozoospermia. The most effective testosterone preparation is not the usual oily solution, but a suspension of crystals of methyl testosterone. Crystals provide a deposit in the gluteus from which hormone is slowly absorbed for up to a week following the injection. In other words, this form of therapy has the same advantage as the implantation of pellets, or tablets, advocated by Deanesley and Parkes, with the additional merit that it eliminates the necessity for a surgical operation and its attendant risk of sepsis. On the basis of Hamilton's findings that pellets require one-fifth of the hormone required when used in oily solution, a weekly total of 9 mg. of methyl testosterone crystals would seem to be necessary. We have found that for clinical purposes 1.5 to 3 mg. given once to three times a week are generally sufficient. The injections cause no local discomfort. The treatment may be indicated in the following conditions:

- (1) Hypoplasia, or inadequate functioning of the ducts, including certain cases of blockage.
- (2) Low invasive capacity of the sperms, and low viability.
- (3) Certain cases of lowered potency and of failure to ejaculate.
- (4) Some types of deficient spermatogenesis associated with sloughing of the seminal epithelium.

RADIOTHERAPY

Successful attempts have for several years been made to stimulate the activity of the ovary by means of carefully regulated X-ray radiation, and this treatment is now being applied to the testicle. Dr. Anthony Green has recently reported to me a case of azoospermia previously treated unsuccessfully with various hormones which responded to X-ray treatment. The regulation of dosage is of the utmost importance, for, as we all know, too large a dose causes degeneration of the tubules.

SURGICAL TREATMENT

I regret to say that the results of surgery in the treatment of sterility are on the whole very disappointing. In my hands the operation of vaso-epididymostomy has not given the high percentage of successes claimed for it in America by Hagner. This may have been partly due to my inability to find in this country the very fine silver wire which he uses as suturing material and on which he places great emphasis. Fortunately I have now obtained from the States a small supply and am hoping for better results. Undoubtedly this silver wire makes a difficult operation much easier. Whatever the technique I am of the opinion that treatment during convalescence with crystalline testosterone is a useful adjunct.

ARTIFICIAL INSEMINATION

Impotence, either partial or complete, is a frequent cause of childlessness, and one gains the impression that sexual difficulties in marriage are on the increase. The vast majority of such cases are psychogenic in origin and yield to appropriate psychological treatment. Some of them, however, prove intractable, and in such cases artificial insemination offers the frustrated wife the possibility of having a child by her husband. This is, of course, only possible if the husband is able to produce semen by masturbation. I have had several cases in which sexuality has been so weak that this was not feasible and I have been trying to discover some means by which an ejaculation could be provoked artificially, but so far without success. There is also another very important type of case in which artificial insemination is of great value. When oligozoospermia and asthenozoospermia exist and treatment brings about no further improvement, it is possible to overcome the scarcity and the lack of vigour of the spermatozoa by safeguarding them from the most perilous part of their journey, that through the lower female passages. In those cases in which bacteria are found in the impoverished semen cultures must be made before resorting to this treatment in order to guard against the possibility of infection. One more point must be noted. In all cases in which we are dealing with low-grade semen there exists the risk that the zygote may die and conception be followed by a miscarriage. Special precautions must therefore be taken against this accident.

THE NECESSITY FOR TEAM WORK

The successful treatment of childlessness requires the closest collaboration between the urologist and the gynaecologist. The increasing use of postcoital tests, and of artificial insemination makes this collaboration a *sine qua non* to success. But not only are the urologist and the gynaecologist involved in the problem of childlessness, but also laboratory workers, radiologists, endocrinologists, physicians and psychologists.

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Post-operative prognosis.—The survival rates and recurrence incidence of the various types of tumour are well known. The adenocarcinoma has a recurrence rate of 60% of these 70% within the first year. In adenosarcoma the survival rate is 5 to 7%, the mortality is 85% in the first year. In tumours of the pelvis 45% die within the first year. What obvious causes can be found for these meagre results? The answer is found again in the natural history of the disease. Adenocarcinoma metastasizes through the blood-stream by the main vessels or by the cortical and capsular circulation. Adenosarcoma recurs locally and invades all structures in its path; epidermoid tumours of the pelvis tend to local implantation on mucosal surfaces. Besides this, a number of patients present themselves for treatment with established metastasis.

Effect of radiation on the tumour.—Radiosensitivity varies both according to the main type of neoplasm and also in different parts of the same tumour. Tumour material, adequately irradiated and examined after an interval of about three weeks shows marked cellular destruction, blurring of the cell outline, transformation of part of the tumour into hyalinized tissue and nuclear changes familiar after irradiation. Yet it must be emphasized that in adjoining parts there may be no alteration in the neoplastic tissues—an important fact which dictates a policy of combined treatment; namely, pre-operative radiation plus nephrectomy, whenever possible, and not radiation as the sole therapeutic measure. Besides these effects on the tumour cells, the peripheral tissues—capsule, perirenal fat and fascia—show fibrosis and sclerosis of capillaries and small blood-vessels. Clinically the radiosensitive types show rapid shrinkage and this is a further indication for pre-operative therapy. Radiosensitivity of adenosarcoma is of very high order, that of adenocarcinoma markedly less so but still considerable, whilst the epidermoid tumour of the renal or ureteric pelvis is radioresistant. It should, however, be remembered that radiosensitivity and curability are not synonymous and that the indication for treatment is not based solely or mainly on the immediate response to radiation, or the rate of regression; therefore radiotherapy to the so-called resistant type not infrequently gives better long-term results than the treatment of sensitive tumours. There is thus evidence that although surgery remains the main form of treatment, radiation is of value as a supplementary or associate measure. The main indications for radiotherapy are as follows: (1) As a pre-operative measure in all cases of adenosarcoma and in those cases of adenocarcinoma where the tumour is of large dimensions or on the borderline of operability. (2) As a post-operative measure in adenocarcinoma and in those cases of adenosarcoma where pre-operative radiation therapy was omitted. (3) As an adjunct to nephrectomy for epithelial tumours of the renal pelvis and ureter where radium is left in the wound at the time of the operation. (4) As the sole method of treatment in inoperable cases, for local recurrences and certain types of metastasis.

METHODS OF IRRADIATION

In cases of adenocarcinoma and adenosarcoma external radiation is the method of choice and is, in fact, the only method for pre-operative and post-operative treatment. Most clinics use X-ray therapy, but telerradium is equally suitable if adequate quantities of radium and the necessary apparatus are forthcoming.

Pre-operative radiation.—When the exact site, its extent and depth from the surface of the tumour-bearing kidney are known, suitable portals are selected; their position and number depending upon the size of the patient as well as the size of the tumour. The tumour rate aimed at is 150 to 250 r per day in adults and about half that dose in children. Most cases are treated at 200 to 250 kV., the physical data varying slightly in different centres, the principle, however, is the same—fractional treatment protracted over an average period of four weeks. The total skin dose per field should not exceed 3,000 r. The optimum time for operation is three to four weeks after irradiation. Delay either in the pre-operative stage or in the surgery following radiation robs the patient of any benefit. The closest co-operation between surgeon and radiologist is essential.

Post-operative radiation allows a greater latitude as regards time and intensity factors; the principles, however, remain the same. In no instance is such post-operative treatment a prophylactic measure, thus, irradiation of the chest with the object of preventing the development of metastasis is not advocated. Post-operative treatment is a local treatment to the perirenal area and to the regional lymphatic fields on the assumption that active malignant cells are present.

In cases of epithelial tumours of renal pelvis, local application of radium at the time of operation is a suitable form of irradiation. Radium foci of 2 to 5 mg., adequately screened and suitably spaced in a rubber container, are placed along the course of the ureter, near the renal pedicle and along the main vascular bundles; the tubes are anchored in position by five catgut stitches; the end of the rubber tubes are brought out of the wound and serve as drains. The dose aimed at is high—5,000 r in the

immediate vicinity of the applicators; this can be achieved in six to seven days, without any risks of necrosis of neighbouring structures.

The treatment of metastasis amounts in practice to X-ray therapy of pulmonary and skeletal lesions. The former have proved resistant and the results are very disappointing. The latter, however, like most osteolytic lesions, give encouraging results with nearly always relief of pain—it is essentially a palliative treatment but the degree of palliation depends upon so many factors that even encouraging local response does not often prolong life or alter the course of the disease. To sum up—the usefulness of radiation in treatment of renal neoplasms is limited; it is not possible at present to claim more than temporary regression of the tumour with pre-operative treatment and of palliation in cases of recurrence. The value of post-operative treatment cannot as yet be assessed.

TUMOURS OF THE BLADDER

Carcinoma of the bladder is a transitional-cell carcinoma. Its three clinical varieties—papillary, ulcerative and nodular—are of similar histological type. The radiosensitivity of these growths is low; by that is meant that a considerable tissue dose is needed to produce regression of the lesion. Of the main forms of radiation therapy, radium or X-rays, radium is to date undoubtedly the more efficacious. X-rays as the sole method of treatment has, in my experience, failed to produce regression; a study of the literature supports this view. The main reason, I believe, is the difficulty to deliver to the tumour in the bladder a dose of X-radiation adequate to control the growth although hæmorrhage may be arrested or controlled. This fact is recognized, and attempts have been made to raise the daily dose to 300 r or more, to use as many as six ports of entry, to push the treatment to the limit of skin tolerance, namely blistering. But these gallant attempts have not resulted in any great improvement, at least with the use of 200-250 kV. There are, however, indications that with higher voltage—600 to 1,000 kV.—and with improvements of both apparatus and technique the position may change. The low voltage, near distance methods such as 90 kV. Chaoul tube or similar apparatus has attracted a good deal of attention. There are inherent drawbacks to this method in the case of bladder growths. Briefly these can be summarized as follows: limitations due to the physical factors of this type of irradiation, chiefly the rapid fall of intensity; this would preclude success on any except the most superficial types of growths (generally adequately dealt with by other methods); limitations inherent to method, namely that the treatment must be given in one session. It is possible to deliver in one treatment of thirty minutes a dose of 3,000 r at the rate of 100 r per minute—but I have yet to be convinced that any form of visceral cancer can be “cured” in half an hour by any machine in existence to-day. The bladder can, of course, be marsupialized or left widely open and the treatment repeated—doses as high as 25,000 r are mentioned in American publications—to this there are grave surgical drawbacks. In my opinion this method is attractive by its superficial brilliancy, but has little future as regards bladder growths.

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As regards technique, the endoscopic method, that is, the introduction of radon seeds through a cystoscope, has naturally attracted the attention of urologists. It is popular in some American clinics; it is suitable in early cases of localized growth in the absence of infection. Only a very few cases fulfil these desiderata.

The advantages of the endoscopic methods are outweighed by the following disadvantages: (1) The wall thickness of the seed is limited by the bore of the instrument, this means that the screenage is limited to 0.3 mm. of platinum; severe reactions follow and risk of infection is increased. (2) The distribution of small radium foci in regular geometrical patterns is difficult, with the result that except in very small lesions, some areas are over-irradiated, whilst others receive a sublethal dose. (3) The falling intensity of radon mitigates against the delivery of the necessary total dose without considerable risk of necrosis.

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The technique of choice is accurate needling under direct vision through a wide suprapubic cystotomy. Suitable retractors, adequate exposure, good illumination pro-

vide the necessary access to the growth. A choice of needles of various lengths, but of similar linear intensity must be available; screenage should be preferably 0.8 mm. of platinum. The actual distribution of the needles depends upon the anatomical configuration of the lesion; most growths can be adequately treated by a single plane implant; patterns previously prepared for different lesions are used. The total dose aimed at is high, namely 7,000 r to 8,000 r. It can be achieved without inflicting burns if the dosage rate is about 35 to 45 r per hour; with such low intensities the total time of irradiation is about nine days. The amount of radium required is small and varies according to the volume of tissue to be treated and its surface extent. The needles must be placed accurately in position and steps taken to ensure that they stay in position. An area of at least 1.5 cm. of apparently normal bladder should be irradiated beyond the periphery of the lesion. Like all surgical procedures, the needling of the bladder requires care, skill and patience; it also requires training and practice. But above all it is not a treatment which can be carried out unless special facilities are available in specially equipped institutions. The closest co-operation between urologist, radiotherapist and physicist is a *sine qua non*. It is this absence of co-operation which has given needling of the urinary bladder rather a sinister reputation associated in the minds of many with burns, cystitis, urgency, frequency, uncontrollable pain resulting in miseries compared with which the natural distress of cancer of the bladder pales into insignificance. I emphasize this point, as it is essential not to gloss over the difficulties or the dangers of the method. Results, however, have justified this treatment and apparently total regressions up to a period of ten years have been achieved. The treatment of cancer of the bladder by radium is as much a surgical procedure as diathermy or excision—it should enlarge and not diminish the urologist's field of usefulness.

Finally attention is drawn to the fundamental differences, in the application of radiation to tumours of the kidney and those of the bladder. The former is in most cases a medical procedure, the latter always requires surgery. The development of these methods and future progress depend upon a clearer conception of what each of the various methods can achieve and on a broader outlook on the part of both urologist and radiotherapist.

Mr. F. G. Stebbing: *Radiotherapy in carcinoma of kidney and bladder.*—Neither surgeons nor radiotherapists have any reason to be satisfied with the results of treatment of carcinoma of the bladder and kidney. Table I shows the total mortality, as recorded

TABLE I.—TOTAL MORTALITY.

Tumours	1942				1943			
	Civilians		Non-Civilians		Civilians		Non-Civilians	
Kidney ...	M.	F.	M.	F.	M.	F.	M.	F.
Bladder ...	354	310	7	—	419	333	5	—
	1,263	595	3	—	1,315	590	2	—

Tumours	1942				1943			
	Civilians		Non-Civilians		Civilians		Non-Civilians	
Papilloma ...	M.	F.	M.	F.	M.	F.	M.	F.
Other benign ...	136	43	3	5	131	30	3	4
Of unstated nature ...	7	1	7	1	8	1	7	1

(From Dr. Percy Stocks, Registrar-General's Department.)

on death certificates in 1942 and 1943. I have put under it the number of deaths from benign tumours of the bladder, because I do not think there is good clinical reason for distinguishing between them. As regards carcinoma of the bladder in 1943 new growths of the bladder accounted for 1,907 out of the 74,000 odd cancer deaths in Great Britain, but if we add the benign tumours we get 2,084, i.e. 2.8%.

Ewing quotes various authors who place the proportion as under 1%.

The disease is more than twice as common in men than in women; the simple tumour being four times as common.

Carcinoma of the kidney accounted for 757 deaths in 1943, nearly equally divided between men and women.

Where carcinoma occurs in an accessible situation, and can be diagnosed early, prompt and radical treatment can effect a very high percentage of recovery as judged by five or more years after treatment, and there can be little doubt that many of those deaths shown in the table could have been avoided if prompt investigation of symptoms had been followed by equally prompt and efficient radical treatment.

The figures of my own clinic at Lambeth Hospital illustrate this well (Table II). Of 102 patients only 12 survived three years and only 6 for five years. The reason for this high mortality was that the great majority of the patients only came to me when disease was so far advanced that palliative treatment alone could be undertaken to relieve their symptoms while they were dying. There are certain things about them

TABLE II.—CARCINOMA OF BLADDER.

Total number of cases treated	1 yr.	2 yrs.	3 yrs.	Alive at the end of				7 yrs.	8 yrs.	9 yrs.	10 yrs.
1931-39 102	32	15	12	4 yrs. 8	5 yrs. 6	6 yrs. 4		3	2	2	1
(Totals only given.)											

to which I would call attention. (1) The great majority of them had had some form of surgical treatment before admission, and in only too many the interval between the first symptom and any attempt at serious treatment was months or even years. (2) A large number of them were treated in the first place as though they were simple papillomata, and the tumours treated by suprapubic or *per urethram* fulguration or diathermy. (3) There was gross infection of the bladder in all but a very small number. (4) Death was due in most of the cases to pyelonephritis, sapræmia with terminal septicæmia, or to hæmorrhage. (5) At post-mortem examination metastases were uncommon; local extension outside the bladder was often seen, but only occasionally were metastases in the liver, lungs or other organs found.

I have been unable to find any records of the mortality in other clinics on the basis of all cases seen; they deal with cases treated only. Gunsett (1931) records 10 five-year survivals of 25 cases. Buschke and Cantril (1942) record 5 survivals out of 52, and Patterson (1941), in his Skinner Lecture, recorded 10 out of 60. It is important to notice that Patterson divided his cases into early and late carcinoma, and reported 58% recoveries in the early group against 7% in the late.

If we are to get the cases early I think the attempt to distinguish between simple and malignant tumours should be given up. Ewing (1940) after reviewing the literature says that it is impossible to tell which papillomata may become malignant and which will remain simple, and quotes Albarran as saying that he found 68 malignant cases to 13 benign. I would suggest, therefore, that all cases of hæmaturia or vesical irritation should be promptly investigated, and, whenever a neoplasm is found, radical treatment, on the assumption that the tumour is malignant, should be undertaken at once.

Patterson gave good reasons for saying that radiation is the method of choice for early carcinoma of the bladder, and I agree with him. If radiotherapy is well planned, and efficiently carried out before there is gross infection of the bladder or extravescical extension, a very high percentage of recoveries can be obtained. Patterson described three methods of radiotherapy: radium or radon implantation through a suprapubic wound, X-ray therapy with low voltage X-rays at a short focal distance through a suprapubic wound, and high voltage deep X-ray therapy. I have no experience of the first two of these methods, and I agree with Patterson that radon seed implantation through the cystoscope should never be attempted, as the efficiency of radiation so obtained is of a very low order.

All my cases have been treated by high voltage X-ray therapy, and I do not find it difficult to build up a high dose in suitable cases by using a 6 by 8 cm. or 8 by 10 cm. beam through six fields. Two anterior, three posterior, and one perineal fields are used. For all but the perineal field the patient is treated with the pelvis raised and the head down, as in the Trendelenburg position; in the perineal field the patient sits on a stool through which the applicator is raised into contact with the perineum. The bladder must always be emptied immediately before each treatment, and a dose of 5,000 r must be delivered to the whole of the bladder in less than four weeks. The difficulties that arise during the treatment are: (1) Infection of the bladder when present must be controlled, as it aggravates the reaction that will be produced. (2) Anæmia which may have been produced by hæmorrhage from the growth must be treated, because the growth of anæmic patients is more radioresistant than those of patients with full hæmoglobin. (3) Skin reactions which may be severe enough to cause some discomfort, but should not be severe enough to be serious. (4) Vesical and rectal reactions which may be severe enough to cause discomfort. (5) Geographical miss, i.e. not keeping the whole tumour in the beam during the whole of each treatment. This is particularly likely to occur with old or unco-operative patients, or if the output of the apparatus is low and treatment unduly prolonged.

Under such treatment large growths, whether benign or malignant, will get much smaller, and often entirely disappear. The bladder should always be inspected at intervals after completion of treatment; Gunsett recommends that any residual growth should be treated by diathermy *per urethram*, but in my experience this is seldom necessary.

When patients are admitted with advanced tumours with gross infection and in poor condition, it is usually impossible to give a radical treatment by radiotherapy, but merely relief of symptoms by a dose of 2,500 r or 3,000 r in less than three weeks. This will generally cause the tumour to shrink, lessen the frequency of micturition and vesical tenesmus, and make the patient more comfortable for a time. The terminal

condition of a patient dying with carcinoma of the bladder with or without a suprapubic fistula is pitiable, and I think it is justifiable when it is recognized that a patient's carcinoma cannot be radically treated to transplant both ureters into the rectum. Radical radiotherapy can sometimes be carried out then in cases in whom it cannot be done without transplantation, and the patient will be much more comfortable even if the growth is only temporarily arrested.

Table III shows my experience with carcinoma of the kidney. The majority of these

TABLE III.—NEOPLASMS OF KIDNEY.

Total number of cases treated	1 yr.	2 yrs.	3 yrs.	4 yrs.	5 yrs.	6 yrs.	7 yrs.	8 yrs.	9 yrs.	10 yrs.	11 yrs.	12 yrs.
1931-39	1	2	3	4	5	6	7	8	9	10	11	12
21	7	5	4	4	4	2	2	2	1	1	1	1

(Totals only given.)

cases came to me after metastases had appeared elsewhere, or after surgery had been done without pre-operative radiotherapy. In most of them also the diagnosis had been made only long after the first symptom had appeared. These tumours are all very radiosensitive, and any given tumour mass, if treated before the growth has broken down or before abscess formation, can be made to disappear. The first difficulty is that metastases in these growths occur early, and the second difficulty is being sure that the growth has disappeared. Kerr and Stevens (1943) report a small series of cases in which the results obtained by pre-operative X-ray therapy followed by nephrectomy were very much better than those treated by nephrectomy followed by radiotherapy, or those treated by radiotherapy alone. They quote Priestley as having reported 35% good results in patients treated by surgery only, while they report 8 living five years after treatment out of 10 patients. This would appear to refer only to patients treated and not to all patients seen.

In neoplasm of the kidney the urological surgeon and radiotherapist should see the case together as soon as the suspicion of carcinoma is entertained. The treatment of choice is to treat the primary tumour by high voltage X-ray therapy delivering 4,000 r in twenty-one days. This can easily be done through a beam 15 by 10 cm. through three fields, anterior, posterior and lateral. Care must be taken to see that the whole of the kidney is included during inspiration as well as expiration, and the field should include the inferior vena cava. Post-mortem examination in patients dying with these growths shows plugs of neoplasm frequently projecting into the veins and often into the vena cava itself, and it is very important that these should be adequately dealt with before surgery. Ten to twelve weeks after the completion of the radiotherapy, a nephrectomy should be performed whether any tumour can be felt or not, and care should be taken to ligature the renal vein close to the vena cava, and remove the greater part of the ureter. The operation is not made any more difficult by the pre-operative irradiation. It is sometimes said that irradiated cases bleed more, and are more difficult owing to adhesions than those that have not been so treated. Neither of these things is true. There is generally less bleeding and there is no increase in adhesions. Where adhesions are found it means that the growth had already extended into the surrounding tissues, and the tumour would have been fixed before the radiotherapy.

Wilms' tumour in infants is exceedingly radiosensitive, and will generally disappear with 2,500 r delivered in fourteen days, but metastases often rob us of a successful result.

To sum up, in carcinoma of the bladder and kidney radiotherapy has a very important part to play, but the best results cannot be obtained unless the urological surgeon and the radiotherapist work in close association from the very beginning of the patient's treatment. I would repeat that if we are to get the best results papilloma of the bladder should be regarded always as possibly malignant and therefore treated as though it were by preliminary radiotherapy followed by diathermy *per urethram* if that be necessary, and that carcinoma of the kidney be treated by pre-operative radiotherapy followed by nephrectomy. For their mutual instruction the follow-up of these patients should be done, wherever possible, by both the radiotherapist and urological surgeon seeing the patients together at each visit.

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Section of Comparative Medicine

President—H. J. PARISH, M.D.

[February 21, 1945]

DISCUSSION ON THE VETERINARY AND MEDICAL CONTROL OF THE MILK SUPPLY

Mr. H. T. Matthews : Like many other things in Britain, the milk industry is evolving slowly from a state in which traditional method and science are almost inextricably mixed. It has been put to very severe test in war and, despite all difficulties, milk-producing farms are now turning out more milk than ever before and the people are drinking more than in peacetime. Over a ten-year period, production is up by about one-third and liquid consumption by two-thirds. Whether this is regarded as a triumph of organization or as an indication of the room for improvement which existed depends on one's point of view. It seems unlikely that this major branch of the nation's major industry will be allowed to slip back when peace returns, which implies the continuance of controls of many kinds. The medical and veterinary attitudes can be stated quite briefly. We shall be dissatisfied until the ordinary housewife can rely upon getting all the safe raw milk she needs for her household and until the farmer who really tries to provide her with it can be assured that his product will not be used for the manufacture of buttons. But the kind and degree of control which we exercise over milk supplies is very small compared with that which, to be effective, must come from within the industry itself.

The idea that either or both medical and veterinary sciences can control milk supplies is reflected in the legislation which is framed to prevent the sale of unsound milk. The industry is a chain composed of three links, production, processing and distribution. The doctor stands at the bottle end, looking after his patient, the consumer. The veterinary surgeon is at the cow end, interested to see that healthy cows produce milk efficiently to provide a living for his client, the farmer. There are numerous other technicians, agriculturist, chemist, bacteriologist, economist, varieties of engineer and so on. Probably the technician who could make the biggest contribution at the present time is the water-engineer but it would hardly be suggested that he should be put in control. Because milk is a food it has been customary to regard all stages in its preparation as falling within the medical province. This is to carry a reasonably sound principle to absurd lengths. It is nearly equivalent to asking the doctor to supervise the cornfield or the poultry farm or even the trawler. Many people will say that medical control of milk supply has failed to prove effective but my point is that the word "control" is wrongly used. Quite frankly I think that if veterinary surgeons had been placed in charge at the distributing end with authority to work all the way back to the farm, it would have proved productive of more all-round benefit during the last quarter of a century. But it would be quite illogical and I hope that it is recognized that no scientist, with his limited view-point, can control from without. I take the liberty of translating the title of our discussion into "The Impact of Veterinary and Medical Sciences upon the Milk Industry".

A review of Government policy was published as a White Paper in July 1943 and given parliamentary sanction in the Food and Drugs (Milk and Dairies) Act, 1944. We still await the Regulations to be made by the Ministers of Health and of Agriculture jointly under this Act, but the general shape of the new structure is clear. The Minister

condition of a patient dying with carcinoma of the bladder with or without a suprapubic fistula is pitiable, and I think it is justifiable when it is recognized that a patient's carcinoma cannot be radically treated to transplant both ureters into the rectum. Radical radiotherapy can sometimes be carried out then in cases in whom it cannot be done without transplantation, and the patient will be much more comfortable even if the growth is only temporarily arrested.

Table III shows my experience with carcinoma of the kidney. The majority of these

TABLE III.—NEOPLASMS OF KIDNEY.

Total number of cases treated	1 yr.	2 yrs.	3 yrs.	4 yrs.	5 yrs.	6 yrs.	7 yrs.	8 yrs.	9 yrs.	10 yrs.	11 yrs.	12 yrs.
1931-39 21	7	5	4	4	4	2	2	2	1	1	1	1
(Totals only given.)												

cases came to me after metastases had appeared elsewhere, or after surgery had been done without pre-operative radiotherapy. In most of them also the diagnosis had been made only long after the first symptom had appeared. These tumours are all very radiosensitive, and any given tumour mass, if treated before the growth has broken down or before abscess formation, can be made to disappear. The first difficulty is that metastases in these growths occur early, and the second difficulty is being sure that the growth has disappeared. Kerr and Stevens (1943) report a small series of cases in which the results obtained by pre-operative X-ray therapy followed by nephrectomy were very much better than those treated by nephrectomy followed by radiotherapy, or those treated by radiotherapy alone. They quote Priestley as having reported 35% good results in patients treated by surgery only, while they report 8 living five years after treatment out of 10 patients. This would appear to refer only to patients treated and not to all patients seen.

In neoplasm of the kidney the urological surgeon and radiotherapist should see the case together as soon as the suspicion of carcinoma is entertained. The treatment of choice is to treat the primary tumour by high voltage X-ray therapy delivering 4,000 r in twenty-one days. This can easily be done through a beam 15 by 10 cm. through three fields, anterior, posterior and lateral. Care must be taken to see that the whole of the kidney is included during inspiration as well as expiration, and the field should include the inferior vena cava. Post-mortem examination in patients dying with these growths shows plugs of neoplasm frequently projecting into the veins and often into the vena cava itself, and it is very important that these should be adequately dealt with before surgery. Ten to twelve weeks after the completion of the radiotherapy, a nephrectomy should be performed whether any tumour can be felt or not, and care should be taken to ligature the renal vein close to the vena cava, and remove the greater part of the ureter. The operation is not made any more difficult by the pre-operative irradiation. It is sometimes said that irradiated cases bleed more, and are more difficult owing to adhesions than those that have not been so treated. Neither of these things is true. There is generally less bleeding and there is no increase in adhesions. Where adhesions are found it means that the growth had already extended to the surrounding tissues, and the tumour would have been fixed before the radiotherapy.

Wilms' tumour in infants is exceedingly radiosensitive, and will generally disappear with 2,500 r delivered in fourteen days, but metastases often rob us of a successful result.

To sum up, in carcinoma of the bladder and kidney radiotherapy has a very important part to play, but the best results cannot be obtained unless the urological surgeon and the radiotherapist work in close association from the very beginning of the patient's treatment. I would repeat that if we are to get the best results papilloma of the bladder should be regarded always as possibly malignant and therefore treated as though it were by preliminary radiotherapy followed by diathermy *per urethram* if that be necessary, and that carcinoma of the kidney be treated by pre-operative radiotherapy followed by nephrectomy. For their mutual instruction the follow-up of these patients should be done, wherever possible, by both the radiotherapist and urological surgeon seeing the patients together at each visit.

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make a very substantial contribution to the dairy industry and, in doing so, to public health.

If the White Paper policy is implemented, the veterinary staff of the Ministry of Agriculture becomes responsible for conditions under which milk is produced. Quite obviously it is not intended that veterinary surgeons are to deal in person with sanitation and equipment, feeding, breeding, milk recording, test sampling and all the other details. The veterinary training fits a man very well to grasp the intimacies of these things though it does not equip him as an expert in all. So it is to be expected that his function will be supervisory and administrative rather than executive, with the most important consideration that his actual visits to the farm must bring the whole of the paper work to life. In the words of the White Paper, "The basis of a sound milk policy, whether from the point of view of the economics of production or the quality of the product, is a well-bred healthy dairy herd". Without claiming any monopoly of knowledge or interest, it is apparent that a very large part of this falls directly or indirectly within the province of veterinary science and I think there will prove to be no intention to exclude other technicians but rather to co-ordinate into a team.

The number and complexity of production problems are such that they are only capable of solution by teams. A few brief examples will illustrate. Foreign and Dominion agriculturists have been impressed with the great gap between the best and worst herds; that there are aristocrats and nondescripts with no middle class. Artificial insemination promises to do something to fill this gap in a comparatively short period of years. J. L. Davies of the Milk Marketing Board, observing the notable increase in liquid milk consumption, estimates that we need to increase the dairy cow population in England and Wales by more than a million. But this is based on an average yield of only five hundred gallons and a milking life of three years, both amenable to very substantial improvement. The range of variation in chemical quality is not less than from $3\frac{1}{2}\%$ to 5% of butter fat, representing, at half a crown a gallon, a value range of about sixpence. If this should come to be recognized by price distinction the Channel Island breeds would increase enormously. When one considers questions of this wider character in addition to the infinite detail of daily routine on a dairy farm it is clear that the producer needs a great variety of technical help and some control. Between the farmer and the housewife there are many chances of good milk being spoilt and few of poor milk being improved. So the responsibility forecast for veterinary surgeons at the source is a heavy one and not such as can be sustained by isolated effort. There are those who say that the key to the milk industry is transport or pasteurization or water supply or some other factor. I think that there are so many keys that no single science or body can handle them all. Effective control will come from within or not at all and the most effective will be economic.

The essential soundness of the new arrangement which stations veterinary science at one end and medical science at the other is fairly manifest. There is, however, a danger of undue separation of functions in practice. An intermediate link would seem to be provided by the National Milk Testing and Advisory Service which is now building up and touches ground common to us both. There are always problems of the health of farm workers, such as the dairymaid with the sore throat and the coughing cowman. It is to be hoped that rigid bounds will not be set by Statute or convention but that we shall meet in person as well as on paper.

I have consciously sacrificed some accuracy of detail and reference to many important aspects in attempting to reduce this very complex subject to simple terms as viewed from the producer's end. One is acutely aware that the weight given to the same factor differs according to one's training and outlook. But it will, I think, be agreed that the kind of control exercised by combined veterinary and medical sciences is vital to the industry.

Dr. W. A. Lethem: There are some 1,500 local authorities interested in milk, but while an authority like the London County Council is responsible for some 30 farms many a rural district council is expected to control 6-700 and a few over 1,000. It is not surprising therefore that supervision is least efficient where it is most wanted. By far the greater amount of disease spread by milk is derived direct from the cow, over which a sanitary inspector has little or no control.

After the last war more attention was given to the production of clean milk, on the mistaken assumption, at least in the lay mind, that cleanliness meant safety. Physical dirt in milk is aesthetically objectionable but it has comparatively little effect on its

of Agriculture becomes responsible for registration of farms and persons engaged in producing milk and for supervision of production. The White Paper states explicitly that the Ministry's veterinary staff will have responsibility for the conditions under which milk is produced. Regular visits by veterinary surgeons to all dairy farms are already instituted, spaced according to many factors. It is certain that the new responsibility will have a more personal touch than Medical Officers of local authorities have been in a position to apply. What can veterinary science contribute at the production end and how will the contribution serve medical interests?

The health aspect stated in terms of human risk reduces down in practice to only two diseases of cattle, tuberculosis and brucellosis and to the occasional epidemics which arise from human agency, not from the cow. Both of the cattle diseases are of such economic importance to agriculture that their control or elimination is called for quite apart from their relationship to human health. Estimates of loss to agriculture are not very reliable but there is no doubt that it is considerable.

Of the measures now in operation against bovine tuberculosis, routine herd examinations, while they do remove large numbers of infective cattle, cannot have a substantial effect upon total incidence until they are conducted with greater regularity and frequency than present circumstances permit. German experience has shown fairly conclusively that the highly organized application of clinical methods more elaborate than we can contemplate in this country fails to clear infection out of a herd. This is not to decry routine clinical work but to recognize its limitations in relation to tuberculosis. The more radical method, utilizing tuberculin, is well established and making progress. The attested and tuberculin-tested herds account for approximately 8% of milk sold through the Milk Marketing Board in England and Wales, probably more in Scotland. The number of cattle in these herds is something over 700,000 and is rising. Vaccination of young stock with B.C.G. is being tried on a large scale. We must admit that we cannot count on any great reduction in bovine tuberculosis for a number of years.

As to brucellosis, the recently introduced system of vaccination with an American strain of the organism is proving so popular that it should not be very long before we have a heavily vaccinated cow population. It is of course too early to predict the eventual effect upon the disease in cattle or on the volume of infected milk although the indications are favourable. An all-out attack upon these two diseases will not be practicable until the veterinary profession is recruited to greater strength. In the meantime medical officers will, no doubt, continue to advocate heat treatment of bulked milk as a safety device, unless it is supplanted by some other method of processing.

It happens that the demands of public health and of agriculture coincide in relation to these diseases. If the primary motive of veterinary science is to make a contribution to agriculture, the human aspect is not ignored. Mastitis is, however, in quite a different category. There seems to be no good evidence that mastitis of the cow constitutes a menace to human health. It is a problem for the farmer and, in some degree, for the distributive branch of the milk industry. The legislation which forbids the sale of milk from cases of mastitis is perhaps based on the supposition that such sale is "prejudicial to the purchaser" or that the milk is "unsound", but not upon any demonstrable transmission of infection from cow to human being. The law is not well observed in this respect and seems to me to be defective on two scores—that it is obscure and that it is not capable of enforcement. To the farmer mastitis presents the most difficult problems and veterinary science cannot yet offer any clear-cut solution which promises to reduce this ubiquitous group of diseases to the level of a minor and occasional malady.

Of the remaining items in the list of pathological conditions which are now scheduled it is at least doubtful whether their retention in legislation framed to protect human health is warranted by experience. Anthrax and foot-and-mouth disease do not seem to constitute a hazard to human health through milk in this country and they are separately dealt with in Orders under the Diseases of Animals Acts. Actinomycosis of the udder is a pathological curiosity if it occurs at all. The morbid conditions of the cow's genital tract and those attended by comæ are farm problems, not those of public health. Difficulties of exact definition suggest that if it is desired to retain prohibiting powers under food and drugs legislation it might be wiser to use an all-embracing term such as "unsound" or "unwholesome", leaving it to case law to test its meaning, than to continue with such a vulnerable list. I think that diseases of dairy cattle could be taken right out of public health legislation and transferred, with modification, into measures designed to benefit the farmer as a producer of an agricultural commodity instead of as a purveyor of human food. Briefed on these lines, veterinary science could

Mr. Clyde Higgs (Dairy Farmer) said that the average farmer looked with grave suspicion on the present-day interest displayed both by the medical and veterinary profession in milk production, and thought that the activities of doctors and vets. would be better restricted to attendance at his bedside or to looking tenderly at his favourite cow. He himself had some sympathy with this view, for he realized the discomfort with which the farmer travelled the straight and narrow path of good milk production. He said good milk production, not clean, for cleanliness was not the summit of perfection. Inspectors of varying creeds and standards popped their heads over the hedges and directed and misdirected him at every cross road. The many interests in the dairy farmers' efforts confused him—how could he understand, for instance, why an attested herd should produce milk of no particular standard of cleanliness or why milk from the same cow, according to its travels, could reach the consumer under ten different designations?

Mr. Clyde Higgs then gave an account of his own experience of dairy farming, extending over more than twenty years. After a few years' unfortunate experience with nondescript Shorthorns, he started to build up a pedigree herd of Ayrshires, with the intention of eventually becoming self-supporting. He had now achieved this aim but the herd was still by no means 100% efficient. He considered that the first step in efficient control of the milk supply was the improvement of the country's livestock. The fantastic prices paid for some animals were quite beyond the reach of the ordinary farmer and did little good because such animals were available to only a very small percentage of farmers. It was, in his opinion, a mistake to match one breed against another instead of deciding on the best breed for British conditions, making it a national one, and doing our best to improve it in every way.

The blood test for contagious abortion was in his experience very efficient but the difficulty lay in preventing reinfection of clean herds from cattle on adjacent farms. When infection occurred in a herd previously free it spread with incredible rapidity. He had now decided to adopt vaccination in his own herd, using the Ministry of Agriculture's vaccine, and vaccinating only those animals which passed the blood test.

His own herd had been attested since 1937 but the interpretation of tuberculin tests at the present time was unsatisfactory and he knew of animals which were classed as reactors at one time and non-reactors later on.

Mastitis appeared to be increasing. Hand milking, even if not done by first-class labour, caused less harm than the best milking machines indifferently handled. The results of bacteriological testing for mastitis were often confusing, animals with obvious mastitis sometimes being reported by the laboratory as free from the disease.

Useless buildings could not be converted into up-to-date cowsheds. It was better to build new cowsheds or even not to have a shed at all. Labour was one of the most vital problems in maintaining a good milk supply. Hired labour could not be expected to work seven days a week and this meant having extra staff. Whilst this was possible for the large farmer it was impossible for the small man, and 90% of Britain's dairy farms were small farms. Co-operation between a group of farms might solve the problem but the British farmer did not readily take to co-operation.

Mr. Higgs described his experiences with the milking bail system and suggested that whilst it was ideal when the land was suitable and at least 50 cows were being milked it could not be recommended for all farms. The best alternative was to have a large covered yard with a small, easily cleaned milking shed, cows which had been dehorned as calves, and less worrying about accurate rationing of the cows.

Until recently he had opposed pasteurization, but he had now changed his opinion. There was always a risk that no matter how healthy the cow, the human element might result in milk which was a danger to the consumer and so he was obtaining a pasteurizing plant to make his good milk better still.

The future of farming in this country lay in mixed farming and the greater part of the mixture should be milk. At present milk represented about one-fifth of the total turnover. Farmers were probably foolish to allow so many Ministries, Departments and other bodies to control the milk supply. It should surely be the pride and privilege of the farmer to produce a first-class article. The Milk Marketing Board should aim primarily at quality and quantity would follow. He would like to see milk everywhere controlled by the producers and so dispose of the multiplicity of controls which now existed. It was the farmer's business to produce milk and to ensure that it was up to the high standard necessary for the nation after the war.

safety and not very much on its freshness or keeping quality. The term clean is misleading and is often used in place of fresh, as souring is caused less by physical dirt than by lactic acid-producing organisms.

The introduction of T.T. and pasteurized milk was a step in the right direction. Curiously enough accredited milk is found to show even a higher percentage of diseased samples than ordinary milk, though this may be due to accredited farmers having on the whole larger herds and hence to a larger quantity of bulked milk being infected from a single diseased cow.

Although occasional lapses are found T.T. milk is on the whole free from tubercle, but is not necessarily free from undulant fever or the organisms of mastitis. Most people hold that all milk ought to be safe, and have a mistaken belief that the occasional prosecution for watering of which they read in the papers indicates that their interests are being properly protected.

All designated milks, T.T., accredited and pasteurized, have to satisfy various keeping-quality tests. None of them is really satisfactory for the purpose. It was at one time thought that coliform organisms indicated contamination with manure, but it is now known that this is not so and that they usually indicate faulty sterilization of the churns or vessels. The count test is very misleading. Milk which has been correctly pasteurized may well show high counts from heat-resisting organisms, which are not only non-pathogenic but also have little effect on keeping quality. The phosphatase test is the only really efficient test of pasteurization. Unfortunately there is no rapid test for pathogenic organisms—for tubercle in particular the inoculation of a guinea-pig and a wait of four or six weeks is usually necessary, though the organism can sometimes be discovered by direct staining of the centrifuged deposit of a very heavily infected milk.

Attention is of course given by local authorities to retail shops. I well remember inspecting dairies in Cornwall some ten years ago to find that the prevailing custom at that time was to sell milk in butcher's shops, in open pans, plentifully besprinkled with flies. The law also requires milk in transit to be protected from unnecessary exposure to heat, though to this day the use of refrigerated vans either on the rail or the road is rare. In the U.S.A. milk has to be kept at under 50° F. until delivered to the consumer and this has led to the use of ice or some form of refrigeration on road vehicles and hand barrows, as is customary here only for ice-cream.

There is of course always the risk of human infection, and although routine measures of hygiene are some safeguard, experience shows that they alone are not enough to prevent occasional outbreaks. The Bournemouth outbreak of typhoid with 51 deaths and 518 cases (among residents alone) in Bournemouth, Poole and Christchurch, and an unknown number outside, was traced to a small farm of six cows in Dorset and although the regulations had not been strictly complied with, it is doubtful if any amount of rural inspection would have prevented the milk being infected. Pasteurization, however, checked the outbreak long before the cause of the trouble was discovered, as it does with all milk-borne outbreaks. The medical examination and certification of milk handlers is impracticable, though a Medical Officer of Health can prohibit the handling of milk by any person whom he suspects to be suffering from a notifiable infectious disease, and milk handlers who have been exposed to such a risk must be notified to him.

Medical Officers of Health are seriously hampered by lack of adequate legal powers. They can stop the sale of milk believed to be infected with any of the human notifiable infectious diseases but not with tubercle, undulant fever or mastitis, except to a school under their own control. And curiously enough it is not an offence to sell such milk even knowing it to be infected. The Tuberculosis Order has done little to protect the consuming public. It takes at least a month to test a sample—and several biological tests are often necessary, so it often takes several months before the cow is discovered, during which time the milk continues to be sold. When the sample is from a bulked supply drawn perhaps from several counties and dozens of farms the search becomes almost impossible. I have received many tragic letters from heart-broken parents pointing out that the milk believed to have infected their children was still being sold and was still known to be infected. I can quote a case where three human cases of undulant fever were traced at intervals of many months to the same T.T. producer-retailer, who refused to have his milk even temporarily pasteurized, and on whose farm, in spite of every effort made by the Ministry of Agriculture, contagious abortion was rife, and for all I know may still be. Actions for civil damages by the unfortunate sufferers are possible, but they are hard to prove to the satisfaction of a court and may be expensive.

supplies. The Ministry of Agriculture should use all means in its power to improve the safety of the milk supply—by encouraging keener inspection of herds, by controlling inspections by biological testing of post-clinical herd samples, by encouraging the keeping of younger herds, and by providing free initial tuberculin testing. Medical Officers of Health could play a part by frequently sampling for biological testing (for tuberculosis) all grades of milk, including pasteurized.

Mr. J. L. Davies : This is about the first time that I have seen prominent representatives of the veterinary and medical professions meeting on the same platform with well-known representatives of dairy farmers. Apart from the consumer these are the three professions primarily interested in the quality of milk.

Even at this meeting some speakers have raised old points of controversy and have tended to frighten us with their desire for still more elaborate control of the operations of the farmer. Such suggestions are easy to make and they have been popular in certain quarters in the past, but I must ask you to bear in mind that dairy farming is an arduous task and our difficulty in the future is likely to be in getting farmers and farm workers to consent to work seven days a week and to produce for us this most valuable product in sufficient quantity to meet our nutritional requirements. Rather than criticize the farmers' efforts we should try to get together to see how we can develop and improve production of milk to give still more satisfactory service to consumers. Much remains to be done before we can say that we have here the necessary basis of an efficient dairy-farming industry—we want to re-fashion and re-equip, and the farmer cannot do this alone.

Let us, therefore, cease to argue about things which are now accepted as inevitable, such as pasteurization or heat treatment of milk when bulked and sold in large consuming areas. Have we not arrived at a point where we are mostly agreed on the main aims of milk policy? The great task which remains for us is devising the means. Here we have a gigantic task, in which we, as farmers, can be greatly helped by the medical and the veterinary professions. It is a creative task of big dimensions, a field big enough for all our energies, and I am sure that we can make progress if we unite forces for this work.

Dr. E. R. Bransby : Safe milk could be provided in two ways, either from healthy cows or by pasteurization with the necessary precautions against subsequent contamination. Cattle diseases cause great loss to farmers and consequently both farmers and doctors would no doubt be agreed about the former of these methods. But the eradication of those diseases in cattle which cause milk-borne diseases in humans is a problem which, even with vigorous action, is not likely to be overcome for many years. On the other hand, there is no physical reason why all milk could not be pasteurized within a short time. I would be glad to know from Mr. Davies, in view of his statement that there is no longer any difference of opinion between farmers and doctors about the provision of safe milk, if farmers would be in favour of compulsory pasteurization.

Mr. H. W. Steele-Bodger : Any measure designed to improve the control of the public milk supply must be capable of practical application. One could legislate against the production of dirty milk, but one could not ensure the production of clean milk by legislation, this could only be effected by education and the payment of a reward. In my opinion the problem could be solved if representatives of the medical, veterinary and farming professions got together and discussed the matter nationally. The medical profession has decided that pasteurization is necessary in the interests of public health but this should not be considered as an alternative to, or a substitute for, animal health measures, but as complementary to them. The late Dr. J. Menton, the Staffordshire County Bacteriologist, has shown by regular biological examinations of milk samples that the quarterly clinical examinations of cows' udders by veterinary practitioners was of value; the percentage showing tubercle infection was 0.6% in designated herds compared with 6% in other herds.

Dr. W. R. Wooldridge : Nothing has been more unfortunate for the progress of safe milk production than the controversy during the last twenty years or more over pasteurization. I am glad to have heard this afternoon from Mr. Davies that milk producers accept pasteurization as a procedure complementary to the production of good, safe

Dr. T. Richards : In order that the plans for the veterinary and medical control of milk shall operate successfully, a few key factors must not be overlooked. The first difficulty is the unenlightened state of so many cowmen and milkers. There is little doubt that veterinary science is already far enough advanced to reduce the incidence of mastitis, contagious abortion and even tuberculosis to almost negligible limits, by segregation, disposal for slaughter, liberal use of hypochlorites in the byre, intelligent use and sterilization of milking machines and other equipment and, above all, good animal hygiene and husbandry. That these diseases still persist, must be due very largely to the fact that in the absence of the veterinarian, his advice and instructions are not carried out and that those who handle milk are so often completely lacking in any sense of hygiene. This state of affairs is not to be wondered at considering the lack of facilities at present available for spreading a knowledge of hygiene among them. In the second place, there is the unsuitability of so many farms for milk production, with their squalid, dilapidated buildings and lack of adequate water and power supplies. The best scientific methods would fail under such conditions. The cost of bringing such premises up to standard, coupled with the already high cost of milk production, presents an alarming picture.

But even on the distribution side of the industry there is a similar lack of hygienic sense and much more energy must be devoted to educational schemes for dairy operatives. Veterinary and medical control of milk will only become really effective when workers are imbued with a sense of hygiene and are interested in producing a hygienic product, and when there is an improvement in creamery conditions, both as regards buildings and overcrowding.

Dr. C. Fraser Brockington : The control of milk from a medical point of view demands the practical application of the principles of epidemiology covering the whole field of milk production up to and including bottling. The time is now ripe to take three further steps in the application of these principles. First, the education of the farm worker in hygiene. The pathogenic organisms which gain access to milk from outside do so largely because of a lack of the most elementary appreciation of hygiene principles among farm workers. The organisms come for the most part from the nose and throat or the bowel, and it should be possible to train a farm worker to appreciate this fact just as effectively as such training can be given to a nursery nurse. I should like to see much more active steps taken in this direction and I believe that the use of films in country districts would constitute a valuable form of training. Secondly, all persons engaged in milk production should be registered if the milk is to be sold raw. Registration should provide for a medical examination which could eliminate dangerous carriers. That many of the outbreaks of typhoid fever are due to chronic carriers can be determined by examination of the stools. Registration should also include a certificate of instruction in hygiene mentioned above. Thirdly, the powers of Medical Officers of Health to stop milk supplies or to order heat treatment when of opinion that they are of danger to health should be strengthened. At the present time the law does not permit this except in circumstances that make it of very little practical value. If these three steps were taken I believe that a great advance would take place in the standards of milk production.

Mr. J. S. Steward said that the limitations and the great potentialities of veterinary inspection of dairy stock were scarcely appreciated. The microscopic examination of milk samples for evidence of udder tuberculosis was remarkably reliable in careful hands—up to 94% were detected microscopically, as checked by biological testing. Clinical examinations would miss up to 50% of cows giving tuberculous milk (i.e. with or without palpable lesions) when checked by biological testing, but when post-clinical bulk milk sampling for biological testing was adopted excellent results were obtained.

Public health obligations were not fully served by animal health projects and some of the conditions scheduled under the Milk and Dairies enactments should be retained. Thus, although uterine or glandular discharge might contain large numbers of tubercle bacilli, yet in the absence of cough or emaciation such cows could not be controlled under the Tuberculosis Order, 1938. It was time that this Order was amended to include all "open" cases of the disease.

The Ministry of Health should create a further designation for milk from abortion-free herds and should educate the public in the meaning of the various grades of milk. The Milk Marketing Board should allow higher premiums for T.T. and School Milk

supplies. The Ministry of Agriculture should use all means in its power to improve the safety of the milk supply—by encouraging keener inspection of herds, by controlling inspections by biological testing of post-clinical herd samples, by encouraging the keeping of younger herds, and by providing free initial tuberculin testing. Medical Officers of Health could play a part by frequently sampling for biological testing (for tuberculosis) all grades of milk, including pasteurized.

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Even at this meeting some speakers have raised old points of controversy and have tended to frighten us with their desire for still more elaborate control of the operations of the farmer. Such suggestions are easy to make and they have been popular in certain quarters in the past, but I must ask you to bear in mind that dairy farming is an arduous task and our difficulty in the future is likely to be in getting farmers and farm workers to consent to work seven days a week and to produce for us this most valuable product in sufficient quantity to meet our nutritional requirements. Rather than criticize the farmers' efforts we should try to get together to see how we can develop and improve production of milk to give still more satisfactory service to consumers. Much remains to be done before we can say that we have here the necessary basis of an efficient dairy-farming industry—we want to re-fashion and re-equip, and the farmer cannot do this alone.

Let us, therefore, cease to argue about things which are now accepted as inevitable, such as pasteurization or heat treatment of milk when bulked and sold in large consuming areas. Have we not arrived at a point where we are mostly agreed on the main aims of milk policy? The great task which remains for us is devising the means. Here we have a gigantic task, in which we, as farmers, can be greatly helped by the medical and the veterinary professions. It is a creative task of big dimensions, a field big enough for all our energies, and I am sure that we can make progress if we unite forces for this work.

Dr. E. R. Bransby : Safe milk could be provided in two ways, either from healthy cows or by pasteurization with the necessary precautions against subsequent contamination. Cattle diseases cause great loss to farmers and consequently both farmers and doctors would no doubt be agreed about the former of these methods. But the eradication of those diseases in cattle which cause milk-borne diseases in humans is a problem which, even with vigorous action, is not likely to be overcome for many years. On the other hand, there is no physical reason why all milk could not be pasteurized within a short time. I would be glad to know from Mr. Davies, in view of his statement that there is no longer any difference of opinion between farmers and doctors about the provision of safe milk, if farmers would be in favour of compulsory pasteurization.

Mr. H. W. Steele-Bodger : Any measure designed to improve the control of the public milk supply must be capable of practical application. One could legislate against the production of dirty milk, but one could not ensure the production of clean milk by legislation, this could only be effected by education and the payment of a reward. In my opinion the problem could be solved if representatives of the medical, veterinary and farming professions got together and discussed the matter nationally. The medical profession has decided that pasteurization is necessary in the interests of public health but this should not be considered as an alternative to, or a substitute for, animal health measures, but as complementary to them. The late Dr. J. Menton, the Staffordshire County Bacteriologist, has shown by regular biological examinations of milk samples that the quarterly clinical examinations of cows' udders by veterinary practitioners was of value: the percentage showing tubercle infection was 0.6% in designated herds compared with 6% in other herds.

Dr. W. R. Wooldridge : Nothing has been more unfortunate for the progress of safe milk production than the controversy during the last twenty years or more over pasteurization. I am glad to have heard this afternoon from Mr. Davies that milk producers accept pasteurization as a procedure complementary to the production of good, safe

milk from healthy dairy cattle. I hope that all parties, including the producer and the medical and veterinary professions, will now get together and use their combined influence to secure the essential conditions, such as proper water supply, adequate power supply, &c., for efficient milk production on the farm. These basic requirements are in the interests of both producer and consumer alike.

Dr. J. T. Edwards (Pirbright): One of the main difficulties in eradicating tuberculosis from cattle in this country is the high incidence of the disease, which makes the cost of eradication prohibitive. When the incidence is low eradication becomes practicable, and this may explain to some extent the large number of accredited herds in certain areas of Wales. The success which has attended efforts in the U.S.A. to eradicate tuberculosis by State-wide tuberculin testing is rendered possible by the low natural incidence of the disease. Local surveys are needed in Britain to determine in which areas the natural incidence of tuberculosis is sufficiently low to enable eradication to be carried out. A local survey made in Banffshire has shown that the incidence of tuberculosis in cattle which were housed in modern cowsheds is somewhat higher than in animals kept under the squalid conditions pertaining among poorer farmers, who own only a few head of milking cows. It seems that housing of any kind is detrimental and the pioneer work of Hosier in Wiltshire has shown that it is both practicable and profitable to keep milking cows under an open-air system. The experience of Mr. Clyde Higgs confirms this view.

The only way to make milk "safe" is to boil it immediately before use. The loss of nutritional value by such treatment is insignificant and readily supplemented from other items in the diet.

Mr. H. T. Matthews (in reply): We have covered a very wide range of ground in discussion and inevitably dealt with some matters of detail which tend to obscure the major theme. So I want to restate my point that really effective control of milk supply must come from within the industry. Fortunately it does not seem that there is any great conflict between industrial requirements and those of public health.

Dr. Lethem has mentioned the difficulty of co-ordinating the fifteen hundred local authorities interested in milk. Probably he referred to England and Wales only. I can underline his observation by citing four adjoining counties which have no less than 348 public health officials, all authorized in some degree to deal with milk. This in addition to numerous other people who visit farms for official purposes.

Pasteurization seems no longer to be a subject of controversy but I would remind those who advocate it as a health measure that it began and will continue as a commercial device. Some years ago its cost was estimated at nearly twopence a gallon which, on present production figures, amounts to well over ten million pounds a year; a notable contribution if it were costed against public health alone.

The education of farm operatives is obviously an important factor in milk control. They are engaged in what is really a highly skilled craft. A few pioneer films are now being shown to farm audiences and received with an interest which seems to indicate that this medium has a future.

Dr. W. A. Lethem, in reply to questions, said that Medical Officers of Health were required to certify that they believed the milk issued to schools to be safe. The Ministry of Food was trying to arrange for the issue to schools of pasteurized or T.T. milk only. Expectant and nursing mothers received an increased ration of whatever milk was available in their district, though most had been warned of the risks of raw milk.

He also said that when the control of farms was transferred to the Ministry of Agriculture, a Medical Officer of Health would still be entitled to visit a farm to investigate human outbreaks under the Infectious Diseases Regulations.

Section of Obstetrics and Gynæcology

President—S. GORDON LUKER, F.R.C.O.G.

[January 19, 1945]

Experimental Foetal Death: The Surviving Placenta

By A. St. G. HUGGETT and J. J. PRITCHARD

(From the Departments of Physiology and Anatomy, St. Mary's Hospital Medical School)

FœTAL death does not necessarily cause placental death. This has been found in many species, including Man. In the rat, with eight young in an average litter, approximately 12% of the fœtuses die before delivery. The fœtal remains are resorbed, but their placenta remain in a recognizable condition for several days.

The placental changes following foetal death have here been investigated experimentally. Death was produced by four methods: (1) Crushing fœtuses through the intact uterine wall at laparotomy, using toothed forceps. (2) Bilateral ovariectomy. (3) Subcutaneous injection of œstrone. (4) Subcutaneous injection of gonadotropic hormone.

The histology of the placenta after spontaneous foetal death was also studied. In all, approximately 180 pregnant rats were employed.

The rats operated upon or injected were at-known stages of pregnancy timed from the discovery of sperms in the routine vaginal smear. After varying periods the mothers were killed and their uteri examined macroscopically and histologically.

The reasons underlying this choice of methods for killing fœtuses will be evident from the following short account of the literature.

Fœtal destruction or removal.—Giacomini (1893) removed the fœtuses in rabbits and found that the placenta continued to grow. Newton (1935) crushed mouse embryos and observed that the placenta persisted and were delivered in an apparently healthy condition at full term. During the period of retention of the placenta the mice remained "physiologically pregnant". With van Wageningen (1943) he demonstrated similar results in the monkey.

Ovariectomy.—The ovaries are required for foetal survival throughout pregnancy in all species investigated except the Horse, Cat, Guinea-pig, Monkey and Man, where they can be dispensed with after formation of the placenta.

In other species the destructive effects of ovariectomy can be prevented by the administration of progesterone. In the five exceptional cases mentioned it has been suggested that the placenta produces the required progesterone (Selye, Collip and Thomson, 1935).

In the rat it has long been considered that the ovaries are needed in all stages of pregnancy. Haterius (1936), however, found that if both ovaries and all fœtuses except one were removed, and all the placenta left in situ, then the remaining fœtus was carried to term. He supposed that between them the placenta produced enough progesterone to supply the needs of one fœtus. Later Haterius and Kempner (1939) showed that paraffin pellets could be substituted for the placenta in this experiment. It was therefore argued that the excess placenta maintained pregnancy by keeping the uterus distended. Recently, the validity of this argument has been disputed by Zeiner (1943) who found that if two-stage ovariectomy was performed with a minimum of trauma, the rat could carry several fœtuses almost to full term, irrespective of the number of placenta in excess.

œstrone.—In 1926 Margaret Smith in the rat, and Parkes and Bellerby in mice, found that injection of ovarian follicular extracts terminated pregnancy. They found that the dose required increased greatly as pregnancy advanced. It was suggested that follicular fluid antagonized the activity of the corpus luteum.

In 1938, Parkes, Dodds and Noble demonstrated the same effects in rats and rabbits after oral administration of synthetic œstrogens.

Gonadotropic hormone.—In the rat and mouse, Engle and Mermod (1928) showed that daily implants of anterior pituitary interrupted pregnancy. In the first third of pregnancy implantation was prevented, in the second, resorption or abortion occurred, but in the last third normal litters were often born.

The ovarian follicles were stimulated by this procedure, and an œstrus type of endometrium resulted. This latter was considered to be incompatible with the continuation of pregnancy.

NORMAL HISTOLOGY OF RAT'S PLACENTA

Pregnancy in the rat lasts twenty-one days and litters average eight. Placentation is hæmochorial, *labyrinthine*, and discoidal. (Man is hæmochorial, *villous* and discoidal.) Implantation of the blastocyst occurs on the 7th day, and is followed by a local decidual reaction which obliterates the uterine lumen. The blastocyst exhibits a mass of trophoblastic cells at one pole known as the *ectoplacental cone*, which is destined to give rise to the ectodermal part of the true or allantoic placenta. Between the 7th and 11th days a yolk-sac placenta is formed with an extensive vitelline circulation. On the 11th day the allantoic mesoderm makes contact with the ectoplacental trophoblast, and with the ingrowth of foetal blood-vessels from the former into the latter (fig. 1), a functional allantoic placenta is established. (The human placenta is composed of the same elements, namely allantoic mesoderm and trophoblast.) At this date also the decidua reaches its peak development, and thereafter rapidly declines, until at the 15th day it is barely recognizable. The yolk-sac, on the 12th day, loses its outer wall, and with the sloughing of the decidua parietalis, the uterine lumen is re-established, lined partly by the surviving inner wall of the yolk-sac and elsewhere by ordinary uterine epithelium.

The fully developed placenta shows three distinct zones. Outermost and adjacent to the decidua basalis is the zone of phagocytic *giant cells*. Next is found a layer of trophoblast which is never vascularized from foetal sources, known as the *reticularis*, while innermost is the *labyrinth* formed from allantoic mesoderm with its foetal blood-vessels on the one hand, and ectodermal trophoblast on the other. The *reticularis* accumulates large glycogen deposits between the 13th and 15th days, but thereafter this zone decreases in size as the glycogen cells disintegrate. The *labyrinth* increases in thickness and complexity until the end of gestation. Terminal degeneration is found in the giant-cell zone at the margin of the placenta associated with the dehiscence of the placenta from the uterine wall preparatory to parturition.

EXPERIMENTAL RESULTS—HISTOLOGY OF THE SURVIVING PLACENTA

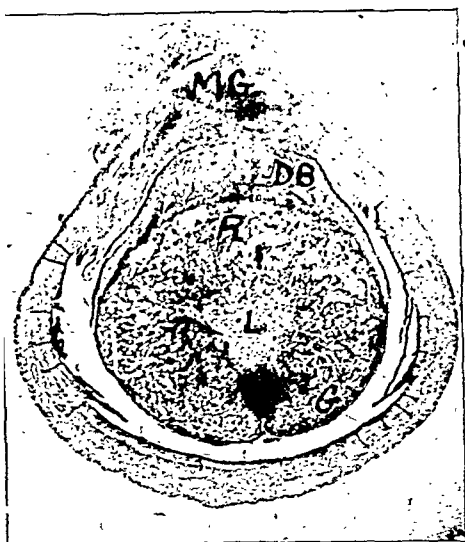
(1) *Crush*.—If the embryo is crushed to death at the 10th day, before the establishment of the allantoic circulation through the placenta, the ectoplacental trophoblast is the only foetal tissue to survive. From 0.5 mm. at its widest on the 10th day, the trophoblast develops into a spherical organ 5 mm. in diameter by the 16th day (fig. 2). Giant cells, glycogen-containing *reticularis*, and *labyrinth* are arranged concentrically from without inwards. The two former zones have normal histology, but the *labyrinth*, besides being free of mesoderm and foetal blood-vessels, shows a varying amount of hæmorrhagic destruction. Those parts of it which survive, however, form a reticulum, with nuclei at the nodal points. The thinning of the trophoblast between the nodes is similar to that found where trophoblast covers foetal capillaries in the normal *labyrinth*.

At the 16th day the glycogen-filled cells of the *reticularis* begin to disintegrate, as in normal development. By the 17th day disintegration is far advanced; this leads to complete destruction of the organ, because the spaces vacated by the glycogen cells become filled with extravasated maternal blood. By the 19th day, a mass of blood clot is all that remains. The decidua, in the "crush" cases, did not involute completely, and was not invaded by the *reticularis* at its centre, as it normally is. Its histology was otherwise normal.

Killing or removing the foetus after the establishment of the allantoic circulation results in survival and growth of the placenta in a more normal fashion (fig. 3). The *labyrinth* in particular is well developed; and though its allantoic vessels are obliterated, its mesoderm continues to provide connective tissue support. The ectoderm proliferates, so that the placenta as a whole grows in size. Under these conditions hæmorrhagic destruction does not occur, and the organ remains healthy to full term.

(2) *Gonadotropic hormone*.—It was found that injection of pregnant mares' serum (P.M.S.) caused foetal death, provided it was given before the 12th day and in a sufficient dose. After that date it was not possible to cause foetal death by P.M.S., except through delay in parturition, which sometimes resulted in death of post-mature foetuses *in utero*.

The 10th day proved the most sensitive and 50 i.u. given then in a single subcutaneous injection caused foetal death in two to three days.

FIG. 2. $\times 8.5$.

"Crush" placenta at 16th day. Operated at 10th.

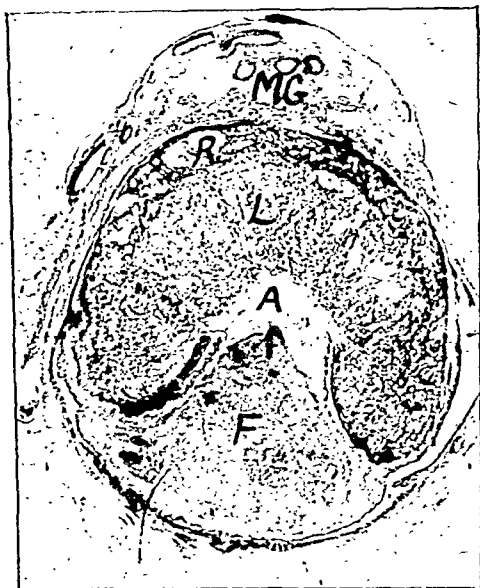
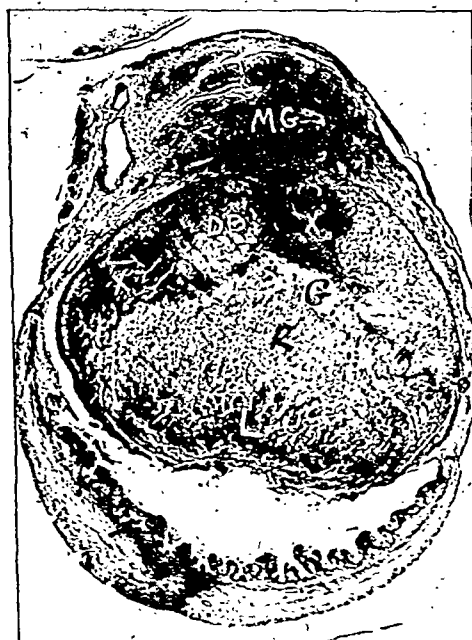
FIG. 3. $\times 8.5$.

FIG. 3.—"Crush" placenta at 19th day. Operated at 15th.

The placenta, however, survived and grew in most cases until the 17th day at least. Histological examination showed that at the time of foetal death, the decidua basalis was necrotic in patches and much reduced in vascularity (figs. 4 and 5). Another finding

FIG. 4. $\times 8.5$.

P.M.S. at 10th. Killed at 13th.

- | | | |
|------|---|---------------------------------------|
| A | = | Allantoic mesoderm and blood-vessels. |
| D.B. | = | Decidua basalis. |
| F | = | Fœtal remains. |
| G | = | Giant-cell layer. |
| L | = | Labyrinth. |
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the giant-cell component. The decidua had failed to involute, remaining the same thickness as at the time of death. It showed poor vascularity, patches of necrosis, and reversion to an oedematous type of uterine stroma, except round the few maternal vessels still present.

(3) *Œstrone*.—Preliminary experiments with œstrone showed that at the 9th day 500, but not 100, i.u. given in a single subcutaneous injection in 50% alcohol, caused death of the embryos. The decidua was found completely necrotic on examination at the 12th day. Later, at the 14th day, as much as 5,000 units did not harm the pregnancy.

(4) *Ovariectomy* (double).—Removal of both ovaries at a single operation gave three different results according to the stage of gestation reached. Operation at the 7th and 10th days caused decidual necrosis within two to three days, with death of the embryos and trophoblast. At the 11th day the decidual changes were less extensive, and the trophoblast survived, though the embryos almost all died and were resorbed. After the 12th day ovariectomy was followed after forty-eight hours by increase in uterine muscle tone, and abortion of several of the litter during the next few days. At autopsy on the 19th and 20th days, two or more living foetuses were usually found *in utero* together with about the same number of dead, crushed and distorted foetuses. The placenta were retained owing to the formation of culs-de-sac off the main uterine cavity on the mesometrial side, which prevented their escape along with the foetuses. They showed all stages from the completely normal attached to living foetuses, to the totally necrotic, where abortion of the foetus had occurred followed by decidual separation. The increased uterine tone showed itself in the elongation of the amniotic sacs and distortion of the placenta from discoidal into conical structures.

(5) *Spontaneous*.—Resorbing embryos constituted 12% of all implantations in one series of 32 normal pregnancies. Examination of the uterus showed that the decidua basalis and varying amounts of placental tissue survived.

In many cases only the decidua remained, and a spherical deciduoma filled the uterine cavity. In other cases the giant cells, reticularis and labyrinthine trophoblast were all recognizable. These placental remnants grew until the 17th day when hæmorrhagic destruction occurred.

From the numbers of resorbing embryos found at autopsy on different days and from the uterine histology, it was deduced that death occurred usually before the 12th day.

CONCLUSIONS AND DISCUSSION

(1) *Cause of death*.—Injections of œstrone and P.M.S. and bilateral ovariectomy in the rat have been shown to cause decidual necrosis leading to death of the embryos, providing they are acting before the 11th to 12th days of pregnancy. After this stage they are ineffective. P.M.S. in addition inhibits the ingrowth of allantoic blood-vessels into the placenta, though it is not certain whether this or the decidual necrosis is the primary cause of death.

The three agencies mentioned have in common a disturbance of the endocrine balance of pregnancy, leading to alteration of the œstrone/progesterone ratio. Many other factors are known which cause death of the embryo by destroying the decidua; e.g. lead and mercury, syphilis and brucellosis, and vitamin-A deficiency. Green (1931) showed a vitamin-A deficiency in the pregnant rat ultimately causes infection in the generative epithelium, leading to puerperal sepsis. This observation was then extended to pregnancy in women. In the rat Mason (1935) carried this further, showing that vitamin-A lack enabled micro-organisms to invade the decidua across the uterine mucous membrane.

Failure of ingrowth of allantoic vessels occurs in other lethal conditions, besides P.M.S. administration. Evans and Burr (1927) showed this to be the cause of foetal death in vitamin-E deficient rats. Chesley (1931) found that foetal mice homozygous for "short tail" (brachyury) failed to form mesoderm, and hence failed to vascularize the placenta. Death occurred at the 11th day and was followed by resorption. Thus a hormone, a vitamin deficiency and a lethal gene all appear to act along a "final common path".

Investigation of spontaneous death in rat embryos showed that most cases were already resorbing at the 12th day. No decidual abnormalities were found. A lethal gene or combination of genes is the most likely cause (cf. Hammond, 1941).

The significance of the 11th to 12th day period in this discussion lies with a number of critical events which occur normally at this time in the pregnant rat. The loss of the outer wall of the yolk-sac, and the vascularization of the allantois involve a change-over from a yolk-sac to a true allantoic placenta. Involution of the decidua, re-opening of the uterine lumen, formation of the metrial gland in the uterine wall, and enlargement of the corpora lutea of pregnancy are other features of this period. Here it may be mentioned that Ewart (1897) showed abortion in horses to be most frequent at the 7th week, when the yolk-sac placenta gives place to the allantoic placenta.

After the 12th day, with the involution of decidua and the establishment of the allantoic circulation, œstrone, P.M.S. and ovariectomy can no longer cause foetal death in their previous manner. P.M.S. now prolongs pregnancy, while ovariectomy causes partial abortion from failure of the uterine muscle to relax before the expanding contents (Selve, Collip and Thomson, 1935).

(2) *Survival of the placenta*.—In whatever manner foetal death is produced, the placenta tend to survive, grow and differentiate histologically, in comparatively normal fashion, especially if the allantoic mesodermal component is present. In the early "crush" experi-



FIG. 5. × 143.
P.M.S. at 10th. Killed at 13th.

- A == Allantoic mesoderm and blood-vessels.
- D.B. == Decidua basalis.
- F == Fœtal remains.
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- R == Reticularis.
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was that the allantoic vessels, had failed to penetrate the trophoblast in their usual manner, so that a functional allantoic placenta was never established (fig. 6).

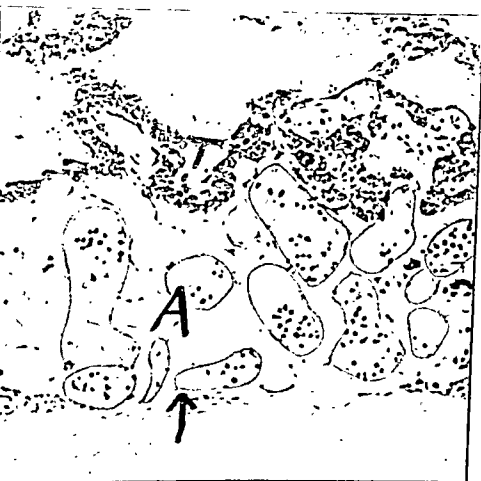


FIG. 1. × 107.
Normal 11th day.

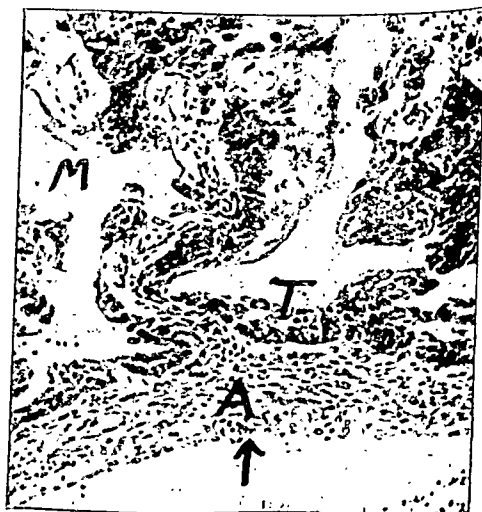


FIG. 6. × 107.
P.M.S. at 10th. Killed at 13th.

The arrows mark corresponding points.

The sections of surviving placenta at the 16th day—where death occurred presumably at the 12th to 13th day—showed that growth of all three zones had occurred, after the manner of the "crush" placenta, but less regularly, with, in particular, overgrowth of

Section of Experimental Medicine and Therapeutics

President—E. N. ALLOTT, F.R.C.P.

[November 14, 1944]

Blood Electrolytes in Clinical Medicine

PRESIDENT'S ADDRESS

By E. N. ALLOTT

THE term electrolyte in clinical acid-base equilibria means such substances as exist in the body, largely in an electrically charged ionized form. The principal electrolytes in the plasma are sodium, potassium, calcium and magnesium, positively charged ions, and chlorine, phosphate and bicarbonate and proteins, negative ions. The proteins of the body have an isoelectric point far to the acid side of the body pH, and at the body pH are negatively charged and are capable of binding a considerable quantity of base. It is necessary to make a few general observations in order that the functions of the body electrolytes in maintenance of osmotic equilibria can be appreciated.

Fig. 1 shows the normal distribution of acids and bases in the blood plasma. Sodium on the base side and chlorine and bicarbonate on the acid side form by far the greater proportion of the plasma electrolytes, and to a very large extent I propose to concentrate on changes in these three ions. Changes in many of the other plasma electrolytes are extremely important, e.g. calcium in various bone and nutritional disorders, potassium in familial periodic paralysis and Addison's disease, but as regards actual maintenance of acid-base balance, they have only a quantitatively minor role to play compared with the three first mentioned.

The electrolytes by virtue of their electric charge, are unevenly distributed throughout the fluids and tissues of the body. The composition of the tissues is entirely different from that of the plasma and extracellular fluid of the body. In the tissues the principal base is potassium, largely neutralized by protein and in many tissues chloride is present only to very small amount. Water and salts can pass freely between the plasma and the interstitial fluid of the tissues, whose composition resembles closely a protein-free filtrate of plasma, and in any changes in electrolyte composition, the plasma interstitial fluids, lymph and cerebrospinal fluid, constitute the "extracellular fluid", which comprises about 20% of the total body-weight. The actual fluid of the tissue cells themselves is in osmotic equilibrium with the interstitial fluid. Water can pass freely between cells and tissues to maintain osmotic equilibria, anions or acid radicals rather less easily, the kations, potassium and sodium pass only with difficulty between fluid and healthy tissues, and protein of course does not normally pass even from the plasma to the interstitial fluid. This unequal distribution of ions is responsible for the maintenance of osmotic equilibria throughout the body. A substance such as urea which can diffuse easily across membranes and is evenly distributed throughout body fluid and cells can, of course, have no value at all in maintenance of body fluid distribution.

I should like to make the suggestion that workers in this country should begin to think and speak more in milli-equivalents when dealing with electrolyte equilibria. It is impossible to add so many "milligrammes" of chlorine to "volumes" of bicarbonate and "per cent." of protein and get a rational answer. The milli-equivalent of any substance is merely its equivalent weight in milligrammes, and is obtained by dividing the number of milligrammes of substance in one litre by the equivalent weight: for example, serum normally contains some 355 mg. of chlorine per 100 c.c., or 3,550 mg. per litre: if this is divided by 35.5 (the atomic weight of chlorine) it gives a value of 100 m.Eq. per litre. This also does away with the confusion which arises through uncertainty as to whether a chlorine value is expressed as chlorine or as sodium chloride; if the serum chlorine value is expressed as 585 mg. (as sodium chloride) per 100 c.c. then the division has to be made by 58.5 (molecular weight of sodium

ments only the trophoblast survived. It grew rapidly, but repeated hæmorrhages impeded the differentiation of the labyrinth and eventually destroyed the whole organ. In the analogous condition of "placental mole" in human pregnancy the growth of surviving trophoblast is similarly impeded by hæmorrhages (Adami, 1909). The placenta surviving later "crush" experiments were more stable and hæmorrhages did not occur. Proliferation of the ectodermal trophoblast resulted in general increase in size, while the persisting allantoic mesoderm acted as a connective tissue framework for the organ.

With oestrone, P.M.S. and ovariectomy, the trophoblast survives in inverse proportion to the amount of decidual destruction. In favourable cases where the flow of maternal blood is not greatly impaired, growth may continue as in the crush experiments. In other cases the trophoblast is partly or wholly destroyed. With progressive necrosis, the labyrinth suffers first, then the reticularis disappears, while finally the giant cells, after an initial hypertrophy, are destroyed. This sequence was also observed by Fortuyn (1920), in spontaneously resorbing mice placenta.

The conclusions to be derived from this are that the trophoblast is relatively insusceptible to agents causing death of the fœtus, that it is nourished from the maternal blood-stream, and from an early stage possesses great inherent capacity for independent growth and differentiation. That the placenta may continue to function as an endocrine organ after foetal death is shown by the positive Aschheim-Zondek or Friedmann tests given by women with "retained products" (Frank, 1929) and by the persistence of such pregnancy manifestations in experimental animals as mammary development, symphysial resorption, water retention, weight increase, and inhibition of œstrus (Van Wageningen and Newton, 1943).

Ballantyne's prophecy in 1902 that we may have to think of the parasitism of the placenta independently of the parasitism of the fœtus has been fully justified by such results as those described.

[The expenses of this work have been covered by a Grant from the Trustees of the Sir Halley Stewart Trust.]

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Mr. Douglas MacLeod said that he and Dr. Harold Burrows had found that human liquor amnii contained large quantities of prolactin-B early in pregnancy but as term approached this gradually diminished, and liquor obtained during labour frequently gave a negative Aschheim-Zondek reaction. Further, injection of liquor obtained by hysterotomy early in pregnancy into pregnant mice at term led to indefinite delay in the onset of labour in every case with gradual absorption of the fœtus and shrinkage of the placenta. It might appear that cases of postmaturity may be explained by the abnormal persistence in high concentration of prolactin-B leading to placental insufficiency and foetal death.

value, but quantitatively this has little effect on the total acid-base balance. In normal blood, sodium forms about 140 m.Eq. per litre out of the total base (sodium + potassium + calcium + magnesium) of 152 m.Eq. per litre, and in discussing changes in body acid-base balances, changes in sodium level represent very closely the changes in total base.

I have not mentioned so far the actual pH of the blood: unfortunately it is one of the most difficult constituents to measure accurately. The body permits of only comparatively slight variations, and the terminal stages of a patient dying in uræmic acidosis and the grossest alkalosis are probably completely covered by a serum pH range of 6.9 to 7.7. Of course, even at the extreme acid pH of 6.9, the amount of ionized hydrogen is far too small to be shown on a diagram such as fig. 1.

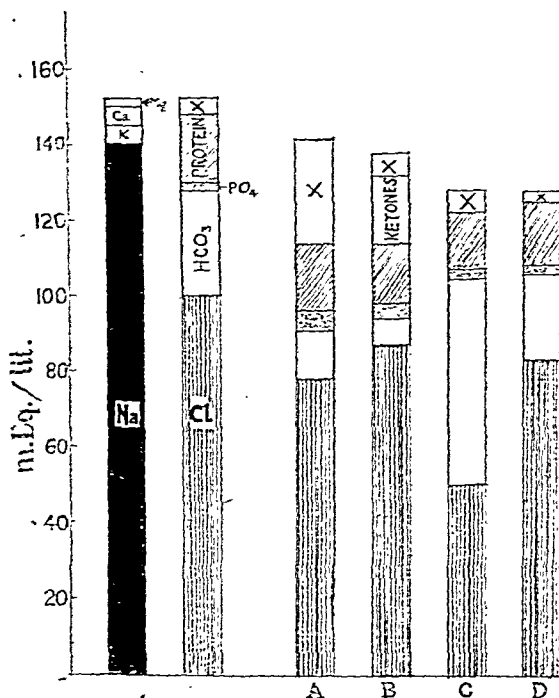


FIG. 1.—Electrolyte pattern of normal serum and anion pattern of pathological sera for comparison. A, Nephritis; B, Diabetic Ketosis; C, Alkalosis; D, Addison's disease. Symbols for the various anions are the same as those indicated on the normal serum.

There is a tendency among clinicians who have not worked much with these metabolic problems to regard changes in sodium and in chlorine as two entirely independent phenomena; they tend perhaps to think of a fall in serum sodium in Addison's disease and a fall in serum chlorine in nephritis. Actually there is in general a reasonably close parallelism between changes in serum chlorine and serum sodium levels in normal and most pathological conditions, provided there is no great change in the alkali reserve. On the whole in untreated Addison's disease the sodium is a little more diminished than the chlorine, while in nephritis, owing to the accumulation of undetermined acids, the chlorine is a little lower than would be expected from the sodium level, but on the whole the sodium:chlorine ratios are within a range which is not very wide.

In reality the fall in serum sodium (together with chlorine) is far from confined to Addison's disease. It is a very common phenomenon in nephritis and in many types of infection, particularly tuberculosis, and is not at all uncommon in patients ill from any cause. In alkalosis, however, the amount of base combined with bicarbonate is so great that the points fall right out of the general run. Fig. 2 shows an unselected series of simultaneous serum sodium and chlorine figures to illustrate these points. In order to assess the acid-base balance of a patient most easily, determinations of the serum chloride and bicarbonate give the most valuable results: variations in the

chloride), which gives the same answer. The conception is used in everyday parlance in connexion with test meals; the expression for the acidity of x c.c. $N/10\%$ is merely a rather clumsy way of saying x m.Eq. per litre.

Table I gives conversion figures for some of the more important electrolytes.

TABLE I.

	Mean normal value as often expressed	Values per litre	Divide by equiv. wt.	Mean normal value in m.Eq. per lit.
Chlorine (as chlorine) ...	355 mg./100 c.c.	3,550 mg./lit.	35.5	100
(as sodium-chloride) ...	585 mg./100 c.c.	5,850 mg./lit.	58.5	100
Sodium ...	325 mg./100 c.c.	3,250 mg./lit.	23.0	141
Bicarbonate ...	60 c.c./100 c.c.	600 c.c./lit.	23.3	27
Calcium ...	10 mg./100 c.c.	100 mg./lit.	20.0	5

For divalent ions, such as calcium, it is important to remember to divide by the equivalent weight, which is half the atomic weight.

In round figures 100 m.Eq. per litre may be regarded as a mean normal value for serum chloride, 140 m.Eq. per litre for sodium and 27 m.Eq. per litre for bicarbonate. The derivation of the base binding power of the proteins is less easy, but in normal blood plasma they may be taken as binding about 16 m.Eq. per litre of base.

As many physicians are still more familiar with values expressed as "mg. per 100 c.c." than in m.Eq./litre, I have deliberately refrained from being entirely consistent and using milli-equivalents throughout, but I hope that before long, this notation will entirely replace the older one when dealing with electrolytes.

The distribution of electrolytes between cells and plasma is so unequal that analyses of whole blood are for all ordinary purposes useless: variation in proportion of cells and plasma merely through anæmia produces very much bigger changes in whole blood composition than the great majority of actual clinical electrolyte disturbances. For accurate work on acid-base equilibria it is essential to collect the blood without stasis, out of contact with air, and to separate serum or plasma out of contact with air. If this is not done, there is loss of carbon dioxide from the plasma, followed by passage of chlorine, with water to accompany it, from cells to plasma, so that appreciable changes from the conditions inside the body are brought about. In an emergency, analyses of clinical value, which might otherwise be missed, can less accurately be made on blood taken without any special precautions; the chloride and sodium values will usually be within 4% of the true value, and the bicarbonate, which suffers most, is not likely to be more than 10% in error, if separated serum is equilibrated with alveolar air, e.g. a true plasma bicarbonate value of say 55 vols. % may be reported as 50. However, for all accurate work, properly collected samples are essential and all figures given in this paper are based on sera obtained and separated without contact with air. Finally, anti-coagulants, with the exception of heparin, cause disturbances in cell-serum electrolyte relations and it is preferable to use serum rather than oxalate plasma for analysis.

Fig. 1 also gives some examples of types of disturbance of the electrolyte pattern of serum met with fairly commonly. For simplicity, only the acid side is shown in the figure: the total base (predominantly sodium) is in all cases necessarily equal to the total acids. One thing common to all is that the body is very much less tolerant of gross variations in the level of serum total base (or, as sodium is by far the main component, of level of serum sodium) than of gross variations in chlorine and bicarbonate. It is possible, for example, in alkalosis for serum chlorine to fall to half its normal value, and provided dehydration is absent the patient may be in fair clinical condition, but a fall of very much less degree in the sodium level is incompatible with life. Diagrams A and B show the electrolyte pattern in two forms of acidosis, i.e. nephritis and diabetic ketosis. They both show a slight fall in sodium or total base, a slight or moderate fall in chlorine, a greater fall in bicarbonate and an appreciable rise in "undetermined acids".¹ In nephritis these undetermined acids comprise a variety of to some extent unknown acid radicals, in diabetic ketosis the rise is practically all accounted for by accumulation of keto-acids. Diagram C shows the condition in alkalosis, typically due to persistent vomiting: here again there is frequently a slight fall in the base, but the acid side of the picture is very different: the fall in chlorine is out of all proportion to that of base, and the missing chlorine is replaced by gross excess of bicarbonate. The final picture (D) is the condition in untreated Addison's disease. Here the fall in base (mostly sodium) is the most prominent feature, the fall in chlorine and slight fall in bicarbonate being only just that required to balance the fall in base. In some of these conditions, particularly in Addison's disease, there may of course be very striking rises in serum potassium, up to, even twice its normal

¹The difference between the measured value of total base and the sum of the measured values for chlorine, protein, phosphate and bicarbonate.

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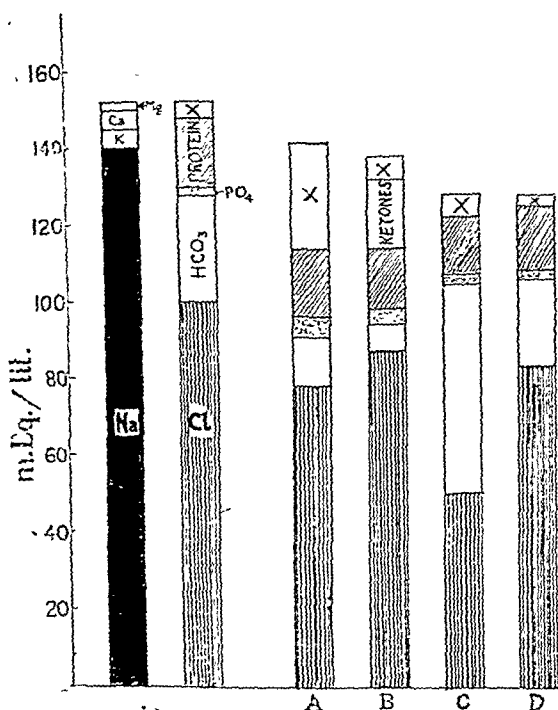


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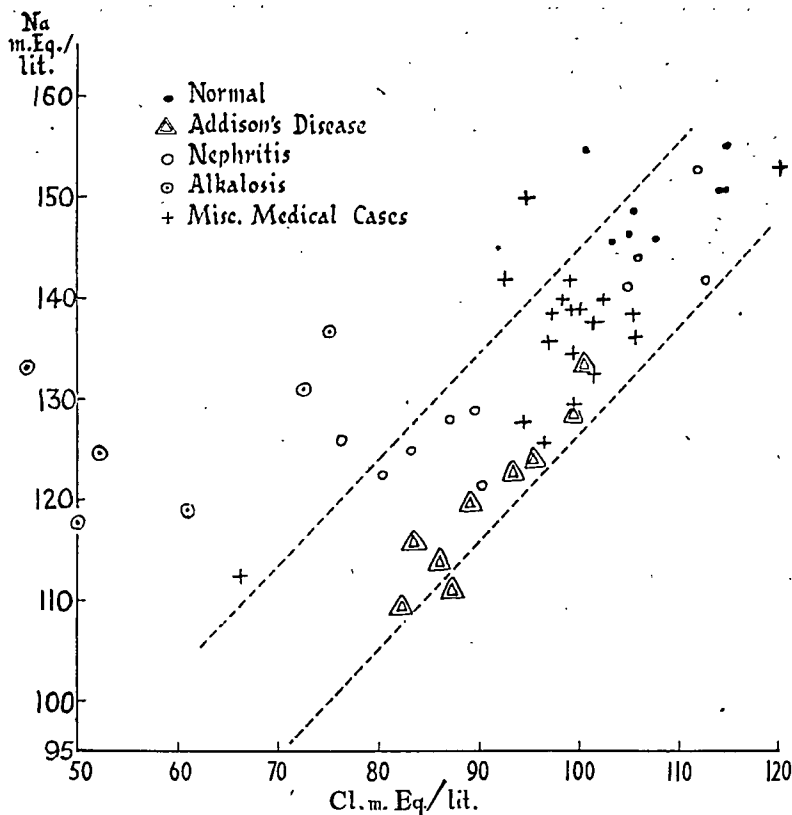


FIG. 2.—Correlation between serum sodium and chlorine levels in normal and various pathological sera.

serum bicarbonate give an indication of the presence of an acidosis or alkalosis, and if the sum of the chlorine and bicarbonate values adds up to 125 m.Eq./lit. or more, it can usually be assumed that there is no gross deficiency of total base.

Generally speaking, when the chlorine level in the serum falls below about 95 m.Eq. per litre, the excretion of chlorine in the urine falls to a low level. This is, of course, the cause of the age-old observation that urinary chloride excretion practically ceases in patients with lobar pneumonia. In Addison's disease, on the other hand, it is well known that high chlorine in the urine can exist with low chlorine in the plasma, and this is the basis of several clinical tests for adrenal cortical insufficiency. What is less generally realized is that the excretion of chlorine in large quantity with low plasma chlorine is not confined to this condition, it occurs, for example, not infrequently in tuberculosis.

Alkalosis, a common clinical example of disturbed electrolyte balance, usually arises through loss of large quantities of gastric secretion in the vomiting of pyloric stenosis. The gastric juice not only contains large quantities of hydrochloric acid, so that the chlorine of the plasma falls and is replaced by bicarbonate, but it also contains appreciable amounts of base, so there is, in addition, in persistent vomiting a fall in serum total base. If the vomiting is due to obstruction, mechanical or otherwise, below the entrance of the pancreatic duct, the vomit may be neutral or alkaline; in this case hypochloræmia, without alkalosis, may develop. All experimental evidence leads to the conclusion that the kidney is interested primarily in maintaining the composition of the plasma, and is not concerned with the total amount of fluid in the body. In order to do this, the kidney excretes water, while retaining as much base and chlorine as possible, and the urine becomes nearly sodium and chlorine free. The loss of fluid by vomiting and in the urine may lead to dehydration, with a rise in blood urea, and although the body may be in a state of marked alkalosis, the attempt to conserve base may produce a strongly acid urine, which only becomes alkaline later as therapy begins to take effect. This secretion of acid under conditions of marked alkalosis was found by McCance to be one of the consequences of experimental salt deficiency, and the

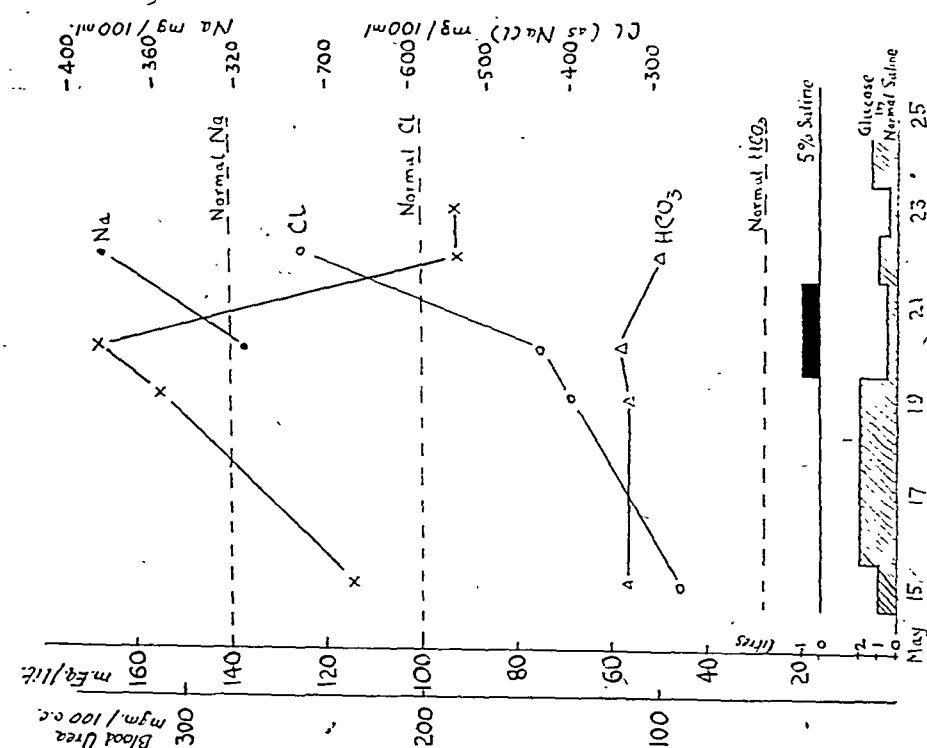


FIG. 5.—Case of alkalosis treated with 5% sodium chloride solution intravenously. Blood urea levels shown by x—x on chart.

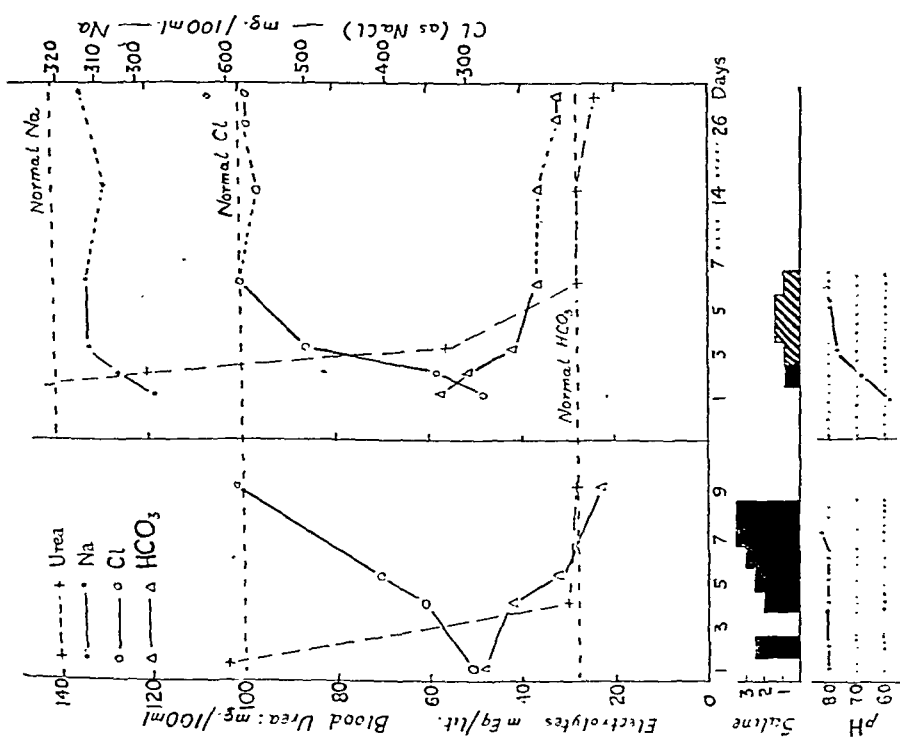


FIG. 3.

FIG. 4.

FIGS. 3 & 4.—Contrasting response to treatment in two cases of alkalosis. The saline marked solid black was given intravenously, that shown hachured was half-strength glucose saline by mouth.

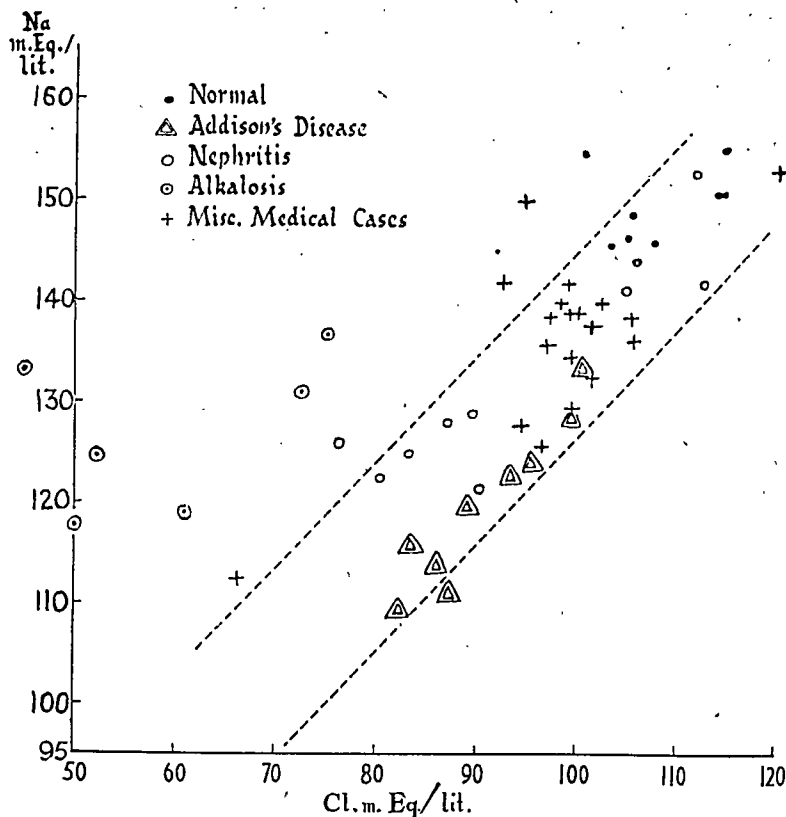


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condition had very strikingly improved. Unfortunately, through a misunderstanding, a further litre of 5% saline was given, and the clinical condition equally rapidly deteriorated: chemical analysis showed now that although the blood urea had fallen to 185 mg. per 100 c.c., the serum sodium and chloride had risen far above normal. As soon as the sodium and chloride figures were known, the intravenous infusion was changed to glucose in water, but he never made a satisfactory recovery. Post-mortem revealed a very widespread inoperable carcinoma, so this therapeutic error had fortunately accelerated the end but slightly.

The second example of the danger of hypertonic saline is a case of Addison's disease. In this case an intravenous injection of hypertonic saline was given by an enthusiastic medical officer to a patient in crisis. He fortunately took some blood for investigation before and immediately after the injection. The clinical condition of the patient was much worse after the injection, and although the same afternoon energetic therapy with adrenal cortical extract and normal saline was given, the patient died. The chemical effects are shown in Table II. The most significant change is the fall in plasma protein, which indicates that fluid has been diverted from the already dehydrated tissues into the blood-stream, but there is only slight change in the sodium and chloride level. The same table shows for comparison, the chemical effect of similar treatment given to a patient with uræmia, and suppression of urine. In this patient there was a definite improvement in the blood chemistry, and a copious secretion of urine following the injection.

TABLE II.—EFFECT OF HYPERTONIC SALINE.

	Addison's disease		Uræmia		m.Eq./lit.
	Before NaCl	After NaCl	Before NaCl	After NaCl	
Serum sodium ...	124.5	127	127.5	133	m.Eq./lit.
" chloride ...	94.5	101	76.7	90	m.Eq./lit.
Plasma total proteins ...	6.8%	5.0%	—	—	

Although the deficiencies of sodium and chloride may not be equivalent, it is most satisfactory to use the neutral salt sodium chloride to remedy the disturbances, provided the kidneys are normal. As shown long ago by Gamble and others, the kidney is capable of retaining what is required to correct the abnormal plasma composition, and of excreting the remainder; there is no value in using acid salts in alkalosis. It has recently been pointed out (Ariel, *et al.*, 1943) as an occasional cause of failure in therapy, that when plasma protein is very low, as for example in carcinoma of stomach, it may be impossible to get the sodium and chloride back to normal unless the hypoproteinaemia is first corrected by plasma or serum albumin administration.

The disturbance of electrolyte metabolism in Addison's disease is due to lack of the adrenal cortical hormones which regulate salt excretion by controlling the amount of sodium and chlorine reabsorbed by the tubules from the glomerular filtrate. In absence of cortical hormone, very little reabsorption takes place, and the body loses salt. In some cases of Addison's disease the administration of large quantities of salt (or a mixture of sodium salts) alone is sufficient to alter the balance, so that a sufficiency is retained in the body, even though reabsorption is imperfect, and a satisfactory clinical and chemical improvement can be obtained by this means alone. In other cases, even the use of large doses of cortical extract as well as salt only produces limited improvement: recently it has been shown that the use of androgens may reinforce the cortical hormone, and produce further clinical benefit. Fig. 6 shows the changes in one Addisonian patient who was treated with 15 grammes salt daily by mouth, with remarkable clinical improvement, and restoration of body chemistry nearly to normal: this patient was never given any cortical hormone, but was able to go home and live a fairly normal life for many months. The second (fig. 7) on the other hand shows a patient who was given, in addition to salt, large doses of a potent cortical extract, and even with that, the restoration of the body chemistry was slow and imperfect, and when the limited supplies of cortical extract available at the time came to an end, her clinical condition rapidly deteriorated in spite of continuation of large doses of salt.

A new syndrome of salt deficiency, resembling adrenal deficiency, but due to a completely different mechanism, has recently been described by Thorn, Koepf and Clinton (1944). This occurs in a certain number of cases of chronic nephritis, where the imbalance of salt excretion is such that the body gradually loses sodium over a long period, and eventually a clinical condition resembling Addison's disease, but without pigmentation, is produced. For a considerable period, some of these patients may be restored to health by administration of sodium salts intravenously or by mouth, but, unlike Addison's disease, the reabsorption abnormality is primarily due to disease of the tubules, and not due to lack of cortical steroids, and administration of cortical extract is without effect. In the end, unfortunately, the patients pass into the more common renal condition, where they are intolerant of salt, and salt therapy leads to

attempt to retain base is the probable cause of a form of renal disorganization noted by McCance and Lawrence as sometimes occurring in diabetic coma.

In general these changes in alkalosis are the easiest of the clinical acid-base disturbances to remedy. The condition is due essentially to mechanical loss of sodium and chlorine from the body, and if these can be replaced by other routes, in general the metabolic upset is rectified. It is necessary, however, to give adequate amounts of salt, and failure is sometimes due to totally inadequate dosage.

If the extracellular fluid is taken as rather more than 20% of body-weight, then a 10 st. individual has 14 litres of extracellular fluid; suppose the chlorine of the plasma (and the plasma findings give a general indication of the condition in the whole of the extracellular fluid) has fallen to 50% of its normal value, a by no means uncommon level, then each litre of extracellular fluid is short of chlorine corresponding to some 3 grammes of NaCl, and if there had been no water shift between the extra- and intracellular phases, $14 \times 3 = 42$ grammes would be sufficient. Actually the water shift is of such magnitude that to remedy the deficiency, the volume of fluid to be taken into consideration is the *whole* body-water, or some 70% of body-weight.¹

A rough useful guide as to the amount of salt required is given by Bartlett, Bingham and Pedersen (1938), for each 100 mg. per 100 c.c. that plasma chloride is below normal, 0.5 gramme of salt should be given per kilogramme of body-weight.

Fig. 3 illustrates a case where the chloride had fallen to half its normal value, and restoration of the normal chemistry of the blood required 17 litres of normal saline, over a period of a week. It also shows another thing: the raised blood urea (104 mg. per 100 c.c.) was restored to normal by relief of dehydration; after only $2\frac{1}{2}$ litres had been given and while the electrolyte composition of the plasma was still grossly abnormal. This patient was comatose at the beginning but rapidly improved as the saline was given: she passed urine with a pH as high as 8.0 right from the beginning, although actually the sodium-content of the urine for the first three days of therapy was too low to be measured.

Fig. 4, in contrast, is an example of another patient whose treatment was largely carried out by giving $2\frac{1}{2}\%$ glucose in half-normal saline by mouth in spite of some vomiting. After an initial 2 litres intravenously, all salt was given orally. The condition of cramps and listlessness present at the beginning responded well, with rapid relief of the tetany and restoration of practically normal blood composition after five days. In this case the amount of salt required was less than would have been expected, only 2 litres normal saline intravenously and 10 litres half-normal by mouth. The rise in the urea clearance from some 15% of normal at the beginning to over 72% on the fourth day is also noteworthy, the blood urea falling from 165 mg. per 100 c.c. to 28 mg. per 100 c.c. over the same period. This patient, in spite of all the manifestations of alkalosis on admission had a strongly acid urine, pH 5.8 to 6.4 in the first four specimens, and it was not until over 2 litres of intravenous saline had been given that an alkaline urine was passed.

Infants are rather intolerant of normal saline, owing to the incapacity of their kidneys to concentrate chlorides beyond a very low level, but this is not any contra-indication to the use of full strength saline in adults. In alkalosis and Addison's disease at any rate I have never seen any harm, and I am not convinced that normal saline, used reasonably, has any serious danger in surgical patients. So long as the urine contains only minimal amounts of chloride, there is little danger of salt poisoning.

To avoid the very large volumes of fluid necessary for adequate salt dosage, hypertonic saline may be considered, and when used carefully in say twice normal strength with adequate biochemical control, has its value, but strong solutions can be extraordinarily dangerous. The next two cases are examples of errors in the use of hypertonic saline with disastrous results.

Fig. 5 demonstrates the effect of hypertonic saline in alkalosis. This patient, aged 41, was admitted in coma, with pyloric obstruction, following a history of dyspepsia and persistent vomiting for some months. The diagnosis of alkalosis was easily made and a drip of intravenous 5% glucose in normal saline at a rate of about 2 litres a day was immediately commenced. Blood taken at the time showed exceedingly gross changes, chloride less than 50 m.Eq. per litre, bicarbonate 56 m.Eq. per litre and blood urea 225 mg. per 100 c.c. After four days of treatment, the clinical condition showed only slight improvement, and the blood urea had risen to 310 mg. per 100 c.c. At my suggestion, owing to the very limited improvement in electrolyte chemistry, and as there was then no clinical evidence of dehydration, it was decided to give some 5% sodium chloride intravenously, and the next day after 1 litre of this, his clinical

¹As intracellular fluid contains essentially no chloride or sodium, this may be a little difficult to understand. It is very clearly discussed by Peters in Duncan, "Diseases of Metabolism." p. 303. (Saunders, Philadelphia, 1942.)

condition had very strikingly improved. Unfortunately, through a misunderstanding, a further litre of 5% saline was given, and the clinical condition equally rapidly deteriorated: chemical analysis showed now that although the blood urea had fallen to 185 mg. per 100 c.c., the serum sodium and chloride had risen far above normal. As soon as the sodium and chloride figures were known, the intravenous infusion was changed to glucose in water, but he never made a satisfactory recovery. Post-mortem revealed a very widespread inoperable carcinoma, so this therapeutic error had fortunately accelerated the end but slightly.

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Plasma total proteins ...	6.8%	5.0%	—	—	

Although the deficiencies of sodium and chloride may not be equivalent, it is most satisfactory to use the neutral salt sodium chloride to remedy the disturbances, provided the kidneys are normal. As shown long ago by Gamble and others, the kidney is capable of retaining what is required to correct the abnormal plasma composition, and of excreting the remainder; there is no value in using acid salts in alkalosis. It has recently been pointed out (Ariel, *et al.*, 1943) as an occasional cause of failure in therapy, that when plasma protein is very low, as for example in carcinoma of stomach, it may be impossible to get the sodium and chlorine back to normal unless the hypoproteinaemia is first corrected by plasma or serum albumin administration.

The disturbance of electrolyte metabolism in Addison's disease is due to lack of the adrenal cortical hormones which regulate salt excretion by controlling the amount of sodium and chlorine reabsorbed by the tubules from the glomerular filtrate. In absence of cortical hormone, very little reabsorption takes place, and the body loses salt. In some cases of Addison's disease the administration of large quantities of salt (or a mixture of sodium salts) alone is sufficient to alter the balance, so that a sufficiency is retained in the body, even though reabsorption is imperfect, and a satisfactory clinical and chemical improvement can be obtained by this means alone. In other cases, even the use of large doses of cortical extract as well as salt only produces limited improvement: recently it has been shown that the use of androgens may reinforce the cortical hormone, and produce further clinical benefit. Fig. 6 shows the changes in one Addisonian patient who was treated with 15 grammes salt daily by mouth, with remarkable clinical improvement, and restoration of body chemistry nearly to normal: this patient was never given any cortical hormone, but was able to go home and live a fairly normal life for many months. The second (fig. 7) on the other hand shows a patient who was given, in addition to salt, large doses of a potent cortical extract, and even with that, the restoration of the body chemistry was slow and imperfect, and when the limited supplies of cortical extract available at the time came to an end, her clinical condition rapidly deteriorated in spite of continuation of large doses of salt.

A new syndrome of salt deficiency, resembling adrenal deficiency, but due to a completely different mechanism, has recently been described by Thorn, Koepf and Clinton (1944). This occurs in a certain number of cases of chronic nephritis, where the imbalance of salt excretion is such that the body gradually loses sodium over a long period, and eventually a clinical condition resembling Addison's disease, but without pigmentation, is produced. For a considerable period, some of these patients may be restored to health by administration of sodium salts intravenously or by mouth, but, unlike Addison's disease, the reabsorption abnormality is primarily due to disease of the tubules, and not due to lack of cortical steroids, and administration of cortical extract is without effect. In the end, unfortunately, the patients pass into the more common renal condition, where they are intolerant of salt, and salt therapy leads to

retention of sodium and water, and the production of œdema. The theoretical interest of this condition is that a similar irregularity of tubular reabsorption can be produced by the two causes, pathological changes in the tubules themselves or insufficient supply of the necessary hormones to enable normal tubules to function properly.

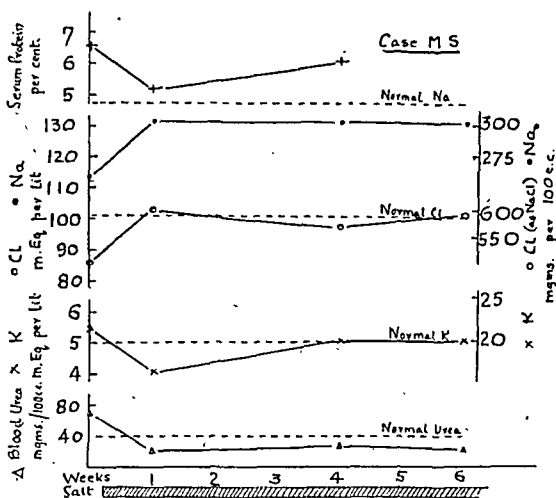


FIG. 6.—Case of Addison's disease showing excellent response to 15 grammes NaCl orally per day without cortical extract.

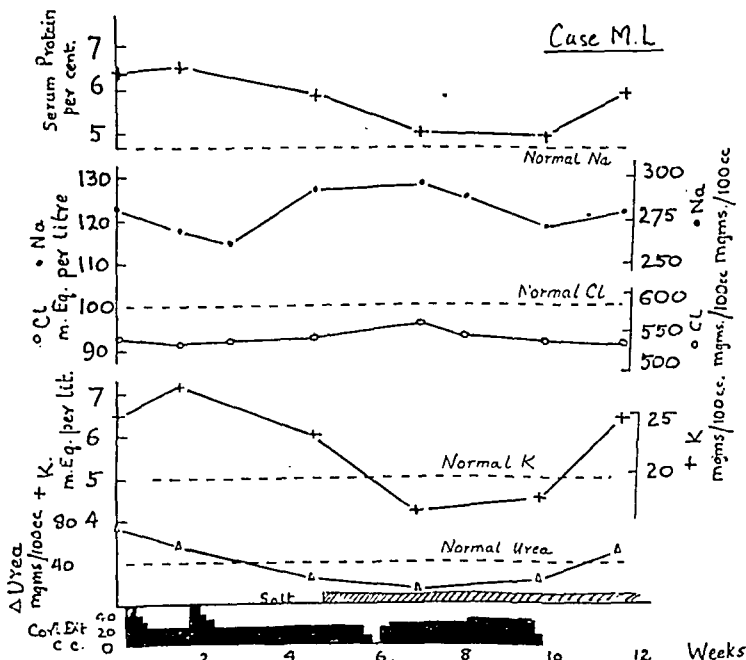


FIG. 7.—Case of Addison's disease, showing poor result sometimes obtained even with large doses of cortical extract and salt.

So far all the conditions I have dealt with have been conditions where there is a deficiency of base and chloride in the blood: the opposite condition does occur, but not nearly so commonly. Routine estimation of cerebrospinal fluid chlorides from time to time produces high values, above the normal limit of 750 mg. per 100 c.c. (128 mEq. per litre). There is little doubt that cerebrospinal fluid is a secretion by the choroid

plexus and not merely a dialysate of plasma, but it is in osmotic equilibrium with the plasma and a high cerebrospinal fluid chloride is invariably associated with a high plasma chloride, and vice versa. When urea estimation is carried out on the blood or cerebrospinal fluid of these patients, it is usually found to be very high, 300 mg. per 100 c.c. or more, and at first sight the patients appear to be examples of a terminal nephritis. Actually the finding of high sodium and chloride levels in terminal nephritis is rare, and the great majority of these patients fall into the so-called "extra-renal azotemia" group. In spite of very high blood sodium and chloride levels, the urine is practically devoid of these elements, although potassium and urea, among other substances, are excreted in high concentration. The cause of this phenomenon is far from clear, but it seems possible that some nervous action, possibly via the pituitary, is involved. A large proportion of patients with this condition whom I have studied have had intracranial lesions of one form or other.

Apart from these cases, clinical examples of high electrolyte concentrations are rare; one example is Cushing's syndrome, where significantly raised figures for sodium and bicarbonate are not infrequently found.

It is perhaps not irrelevant to say a few words about the significance of low cerebrospinal fluid chloride: invariably low cerebrospinal fluid chlorides are due to low chloride content of the plasma. A fall in cerebrospinal fluid chloride content does not in any way indicate meningitis; it occurs in any condition where plasma chlorides are low for any reason. This may sometimes cause confusion clinically in an infection where there may be symptoms of meningism; for example, lobar pneumonia is nearly always associated with a fall in cerebrospinal fluid chlorides, entirely apart from any meningeal infection. Low chloride content of the cerebrospinal fluid is not evidence of meningitis unless there are at the same time signs of meningeal inflammation such as a rise in the cell count and protein content of the fluid.¹ The lowest cerebrospinal fluid chlorides, like the lowest plasma chlorides are found in alkalosis: the lowest I have personally seen in this condition is 72 m.Eq. per litre (422 mg. per 100 c.c. as sodium chloride); many cases of nephritis also show a marked fall in the cerebrospinal fluid chloride level.

Tuberculous infection generally is associated with low plasma chlorides, and this is reflected in a low cerebrospinal fluid chloride, whether there is or is not meningitis. In tuberculous meningitis, on the whole, the chloride content tends to be lower than in ordinary coccal meningitis, but contrary to a widespread belief there is no sharp dividing line between the two. I have gone through our laboratory records for ten years, and fig. 8 shows the contrast clearly. The figures shown are the results of the

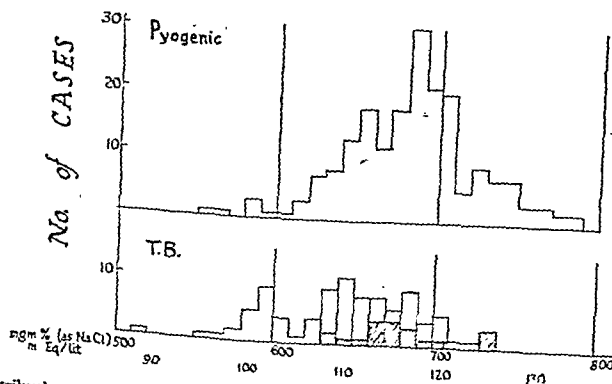


FIG. 8.—Distribution diagram of chloride values in first specimens of cerebrospinal fluid from pyogenic (chiefly meningococcal) and tuberculous meningitis. Shaded portions of the columns among the tuberculous meningitis indicate cases where a lower reading was found on later specimens.

first cerebrospinal fluid examination on each patient; in some cases, shaded in the figure, a lower value was obtained on subsequent examination, and doubtless if examinations had been repeated more often, a further fall in some might have been observed towards the end, but from the diagnostic point of view, the values early in the disease are the most important. If the figures are looked at in another way, it may be said that approximately 50% of cases of tuberculous meningitis have cerebrospinal fluid

¹Very rarely cases of tuberculous meningitis are met with, where there are only 3-4 lymphocytes per c.mm.

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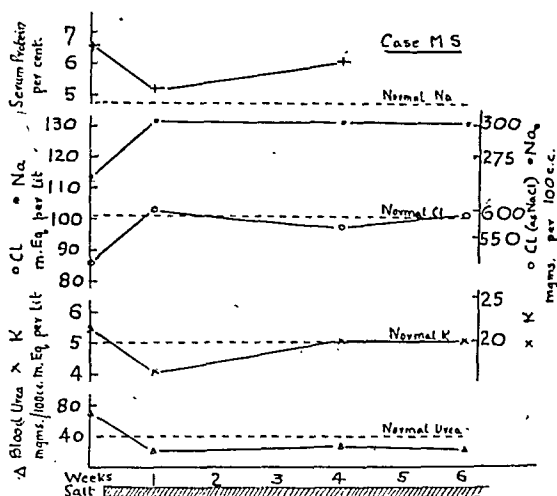


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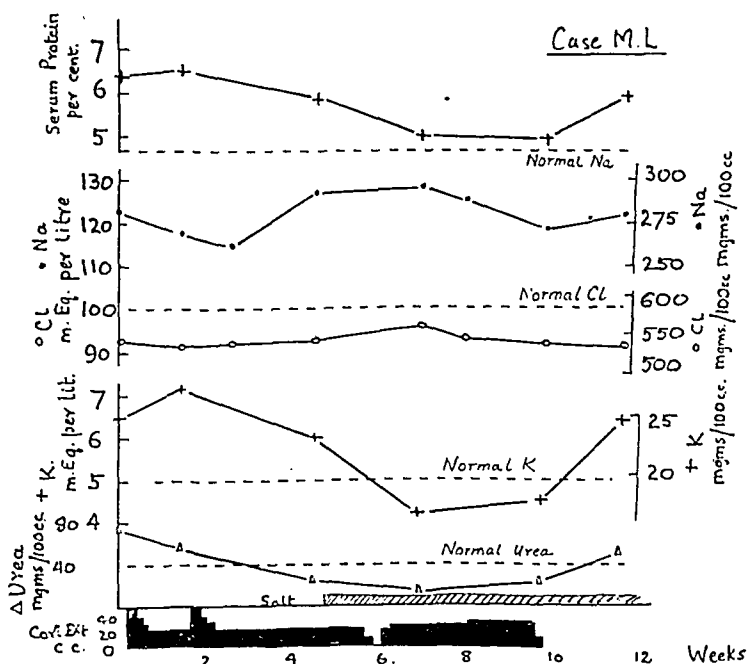


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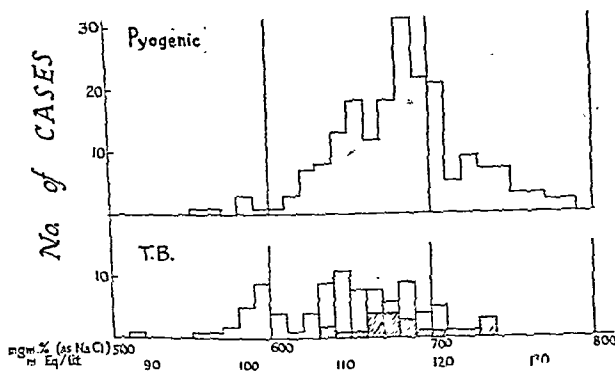


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chlorides of 640 mg. per 100 c.c. or lower on admission, whereas 50% of non-tuberculous meningitis have chlorides of 675 mg. per 100 c.c. or lower, 25% of the tuberculous patients have chlorides of 600 mg. per 100 c.c. or lower, while only 5% of non-tuberculous are as low.

Although sodium, chlorine and bicarbonate are the electrolytes chiefly concerned in acid-base balance of the body, it is perhaps appropriate to include a few very brief remarks about clinical changes in serum potassium. As regards the other kations, changes in calcium metabolism are too well known to require mention, and there is very little known at present about changes in serum magnesium.

Some years ago I showed that serum potassium fell to very low levels in attacks of familial periodic paralysis, the first example where a fall in serum potassium was shown to have any clinical importance. This fall appeared to be due to an abnormal muscular demand for potassium, as we were subsequently able to show by balance experiments that the urinary excretion of potassium at the time of an attack fell to very low levels. Up to the present, familial periodic paralysis is the only authentic condition in which paralysis is associated with low serum potassium: I have repeatedly found serum potassium as low as 7 mg. per 100 c.c. (less than 2 m.Eq. per litre) in alkalosis, without any symptoms, and the low finding after testosterone administration or in Cushing's syndrome is not associated with any paralytic manifestations. A recent paper by Brown, Currens and Marchand (1944) describing attacks of paralysis in association with chronic nephritis, and claiming that these are due to loss of potassium is not convincing.

High serum potassium occurs notably in untreated Addison's disease, in some cases of crush syndrome and in some cases of chronic nephritis with uræmia, although, frequently, a damaged kidney retains the property of excreting potassium adequately after it has lost the power of dealing with sodium. In general, moderate rises in serum potassium level produce no symptoms, but very high values above about 10 m.Eq. per litre (39 mg. per 100 c.c.) are associated with electrocardiographic changes and perhaps terminal heart failure.

These examples have been chosen to depict the changes occurring in some of the serum electrolytes as related changes between the parts of a very delicately balanced mechanism, rather than as isolated, unrelated, phenomena, and no attempt has been made to cover completely the metabolism of sodium and chlorine.

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Section of Proctology

President—R. S. CORBETT, M.Chir.

[November 8, 1944]

A Review of the Surgical Treatment of Chronic Ulcerative Colitis

PRESIDENT'S ADDRESS

By R. S. CORBETT, M.Chir.

UNDER the term "Ulcerative Colitis", this disease was first described as a "pathological lesion" by Wilks and Moxon in Lectures on Pathological Anatomy in 1875. Thirteen years later, in 1888, appeared the first clinical description by Sir William Hale-White. From this time little was written on the disease for many years. In 1909 a symposium on "The Non-specific Type of Ulcerative Colitis" was held under the aegis of this Society and cases were reported from six of the teaching hospitals in London. The total number of cases collected at that time were 160 and the deaths amounted to 71—a mortality of 44%. This shows that it was a serious disease, and one attended with a high mortality. The next discussion here came in 1923, when the late Sir Humphry Rolleston summarized the situation by stating that ulcerative colitis was not a disease in the strict sense of the word, but rather a syndrome with fairly constant changes, which may be brought about by different factors. Mr. Lockhart-Mummery noted at that time the fatal consequences of the disease and the small advance that had been made—both in diagnosis and treatment.

In 1924 there appeared in the Collected Papers of the Mayo Clinic the work of J. Arnold Bargen. In this paper he put forward the suggestion that the disease in many cases was associated with an infection by a specific organism, closely resembling a hæmolytic streptococcus, which is now referred to as a diplococcus.

In 1936, this Section invited Dr. Bargen to give us a paper on "The Management of Chronic Ulcerative Colitis". It was interesting to hear from the fountain head the findings of the diplococcus, which was considered by him to be the causative organism in 80% of cases. At this time he stated that 85% were treated by medical means and 15% required surgical interference. The type of operation carried out then was ileostomy with a 50% mortality.

In 1940, with Mr. Lockhart-Mummery as our President, this Section discussed the surgical treatment of idiopathic ulcerative colitis and its sequelæ. There was strong support for appendicostomy by Mr. Lockhart-Mummery, Mr. Norbury and Mr. Gabriel. On the other hand, the advantages, and the lack of discomfort of an ileostomy were reported by Mr. Ogilvie, the late Sir Arthur Hurst and myself.

There is no doubt that appendicostomy was the most popular form of surgical treatment in London only just over four years ago. It is of interest to follow up some of the cases treated surgically and sum up the results.

DIAGNOSIS

We now regard chronic ulcerative colitis as a definite entity; a chronic infection subject to acute and subacute exacerbations. Clinically, its main feature is diarrhœa and the stools contain not only blood and mucus but also pus. A secondary anæmia is always present and there is a loss of weight, with fever. This is frequently followed by periods of remission and there is a tendency to complications.

The X-ray appearances show an irritated hyperactive colon with loss of normal haustrations and constant narrowing, the appearance often being described as "pipe-stem" (see fig. 7a and 12a). This may not be permanent, as was shown by Sir A. Hurst

in skiagrams taken before and after nine months' medical treatment, when the haustrations are seen to return.

Sigmoidoscopic appearances.—Sigmoidoscopy is essential in establishing an accurate diagnosis. Since the progress of the disease is from rectum to colon in the vast majority of cases, the early and late appearances can be accurately established by this investigation. First, the bowel is seen to be hyperemic, and later, there is œdema and thickening of the mucous membrane, which bleeds easily. A further stage is the formation of military abscesses in the mucosa which rupture and result in ulcers, resembling yellow spots scattered all over the wall of the gut. Finally, the muscular coat is exposed and the ulceration extends so that only islets of mucous membrane are left. These become œdematous and, as Hale-White said in 1888 "a careless observer concludes that the islets of mucous membrane are polypoid growths and the exposed muscular coat is the natural level of the colon." So the pseudopolyposis is formed. Final changes are seen in the photographs of post-mortem specimens kindly lent by Dr. Cuthbert Dukes (fig. 1).



FIG. 1.—Advanced pathological changes in colon. Taken from post-mortem specimens (kindly lent by Dr. Cuthbert Dukes).

ÆTIOLOGY

This is still very obscure. Pathologists in this country do not consider Bagen's diplococcus to be a specific cause of the disease. It is true that the coccus can be isolated from cases of ulcerative colitis and grown from the ulcers, but it can be recovered from other cases of diarrhœa. It is also normally present in the bowel. Another view is that the disease is caused by the *Bacillus dysenterix*. There is no doubt that the true dysenteries are closely allied to this disease and it is of extreme importance to exclude any of the specific forms of colitis. This especially applies to the amœbic form which, though rare in this country, does crop up from time to time and closely simulates the clinical picture of chronic ulcerative colitis.

To sum up, the causation of the disease is not known. It is characterized by a very varied clinical and pathological course. It is subject to exacerbations and periods of remission and complications are very likely to occur. It is a disease in which emotional upset may be an important factor in the ætiology (referred to by Cullinan and Witkower).

GENERAL TREATMENT

There is no doubt that medical measures must be instituted first and adequately carried out. This entails patience and perseverance by both doctor and patient. Only when these measures fail and it is seen that the patient is losing ground in spite of them, or that complications arise, should surgery be considered. The diversity of opinion with regard to diet, medication and the many solutions used for irrigation or given as enemata, and even the introduction of oxygen into the colon, show that the physician

are not satisfied with any one form of treatment. There is no doubt that a number of the milder forms of the disease do respond well to conservative measures.

INDICATIONS FOR SURGICAL TREATMENT

Most authorities will group these under three general headings: (1) Acute fulminating cases. (2) Chronic cases which do not respond to medical treatment or which recur in spite of medical treatment. (3) Cases associated with complications.

(1) *Acute fulminating cases.*—If surgery is carried out, it is attended with a very high mortality, but without it the patient will probably die; and if there is a small percentage of recoveries, it seems to me that one is justified in considering some form of surgical treatment in this group. The risk being so very great, operative interference should be limited to the simplest possible procedure. In children the risk of operation is very great.

(2) In the second group, the difficulty lies in deciding at what stage in the course of the disease the operation should be carried out. If left too long, the condition of the bowel is so serious that whatever surgical operation is performed, the final result will not be satisfactory. Another school suggests that operation should be considered at an early stage and so allow the bowel to recover and make it safe to return to its normal function and avoid a permanent fistula. This then should be done before irreversible structural changes in the colon occur, such as we have seen in the post-mortem specimens.

(3) There is general agreement that surgery is definitely indicated in all cases associated with serious complications.

Complications of the disease.—According to figures from the Mayo Clinic complications occur in about 15% of cases and are divided up into two groups:

A major group including conditions such as polyposis (fig. 2), stricture, arthritis, perirectal abscesses and fistulae, cutaneous lesions, perforation and carcinoma (3.2%).



FIG. 2.—Skiagram of colon showing an advanced stage of the disease. The translucent areas suggest the presence of polypi. (Kindly lent by Mr. Gabriel.)

A minor group including thrombosed and prolapsed hæmorrhoids, anal fissures, pruritus, tetany, clubbing of the fingers (hypertrophic osteoarthropathy) and infantilism—when the disease occurs in young children.

SURGICAL TREATMENT

Appendicostomy.—In 1895 Keetley suggested the use of the appendix for irrigation purposes but it was not until 1902 that Weir performed the first appendicostomy for ulcerative colitis. The operation is simple—and gives rise to very little upset to the individual.

The advantages of this operation are: (1) Simplicity attended with very little risk to the patient. (2) It allows irrigation of the colon, which can even be carried out by the patient himself. (3) Easy removal of the appendix when not required for further treatment of the colon.

The disadvantages are: (1) It does not allow absolute rest to the colon as it affords no

exit for colonic contents. (2) It does not always act as a satisfactory entrance for irrigating fluids. Alternatively, it sometimes causes constant leakage, even *with* a catheter and spigot in situ. (3) If allowed to close, or to become obliterated, the colonic lesion is very apt to recur. (4) If subsequent surgical procedures have to be considered, it is a disadvantage both to the patient and the surgeon. (5) There is danger of death from peritonitis arising from the appendix stump in the course of irrigation treatment.

The figures given in the last ten years in this country show a mortality from this operation of about 20%.

Cæcostomy.—In 1900 Bolton performed the first cæcostomy; it was of the "valvular" type (after Gibson and Senn) similar to that carried out in gastrostomy. This type can be considered as an alternative to appendicostomy, when the appendix is absent, or not suitable. The same disadvantages and advantages can be stated.

The other type of cæcostomy is the "open" type which leaves a free opening on the surface of the abdomen and has the advantage over the valvular type in that drainage of the colon is provided in addition to allowing irrigation to be carried out. Also, an easy secondary closure can be effected when it is felt that the bowel has sufficiently recovered. In 1928, Santee, of the Belle Vue Hospital, New York, strongly supported this type of cæcostomy. He felt that this operation fulfilled the three essentials: (1) The application of rest to the involved colon. (2) The opportunity for irrigation. (3) The opportunity for closure without danger when the gut had returned to nearly normal. He reported four patients treated in this way: two were closed—one in eleven weeks and one at the end of six months. We do not know how they fared after that.

Both appendicostomy and cæcostomy have the same object—the treatment of the colon by means of irrigation.

Are irrigations the best way of bringing about healing in a diffusely diseased rectum and colon, and is it not possible to carry out equally good irrigation *per rectum* if this form of treatment is thought to be indicated? Hurst has shown that from radiological experiments the cæcum can always be reached by running in a pint and a half of fluid *per anum* and that the colon is completely evacuated by this means—especially in an irritative lesion like ulcerative colitis. My own impression about irrigation is that the ulceration of the colon has as good a chance of healing when it is kept absolutely at rest without irrigation or instillations of any sort. Even when the colon is at rest the inflammatory process does not always cease, as we shall see when we review the results of ileostomy alone.

Colostomy.—Colostomy has no real advantage over the previous procedure except that it puts the diseased portion absolutely at rest and allows functional activity of the proximal colon. A transverse colostomy can be considered in those patients who suffer from an involvement of the left half of the colon only. I was tempted to establish a transverse colostomy on a girl of 19 who only appeared to have involvement of the rectum and sigmoid. Medical treatment had failed to arrest the disease and the barium enema showed involvement of the left colon, which was confirmed by sigmoidoscopy. Immediately after the operation a great improvement resulted but the local condition persisted in spite of rest and the additional treatment of sulphonamides locally. After two years the patient returned to hospital suffering from bilateral perirectal abscesses from which she nearly died.

A firm indication for this operation is in regional colitis. This forms a distinct group, though a small one, estimated at 7%. It probably has a very different underlying pathology. It is well treated with a temporary colostomy which should in all cases be followed by a local resection.

OCCCLUSION OPERATIONS

Complicated procedures involving a temporary colostomy have been advocated from time to time and will be considered under "Ileosigmoidostomy".

Ileosigmoidostomy is not a satisfactory initial procedure. It has a place in the final phase of treatment associated with colectomy, when the sigmoid colon has recovered from the disease processes and the patient wants to be rid of the fistula.

If we are right in assuming that in the majority of cases the disease starts in the rectum and spreads up along the colon, it seems likely that the constant flow of ileal contents will bring about a marked irritation of the rectum, with a probable recurrence of symptoms worse than the original disease. In a few cases where the rectum and sigmoid appear to recover when there is still ulceration in the rest of the colon, then ileosigmoidostomy might be justifiable.

It is curious, however, that according to some reports, when this operation is carried out in the early stages, the ileal contents, instead of irritating the rectum appear to

encourage healing, and the rectum recovers rather than gets worse, as in the following report:

In 1925, Reinhoff, W. F., reintroduced the operation of ileosigmoidostomy to eliminate ileostomy. He quoted two cases—the first had an ileostomy and appendicostomy with little improvement. Six months later an ileosigmoidostomy was carried out and the appendix removed. One year later the patient was very fit and reported cured. The first step may have had some bearing on this result. In the second case the operation was carried out as a primary procedure, no previous operation being done. Four weeks later the rectum was stated to be free from ulceration.

In 1931 there was a paper by Arn referring to the treatment of five refractory cases by ileosigmoidostomy, combined with distal ileostomy (fig. 3, *a* and *b*). They all

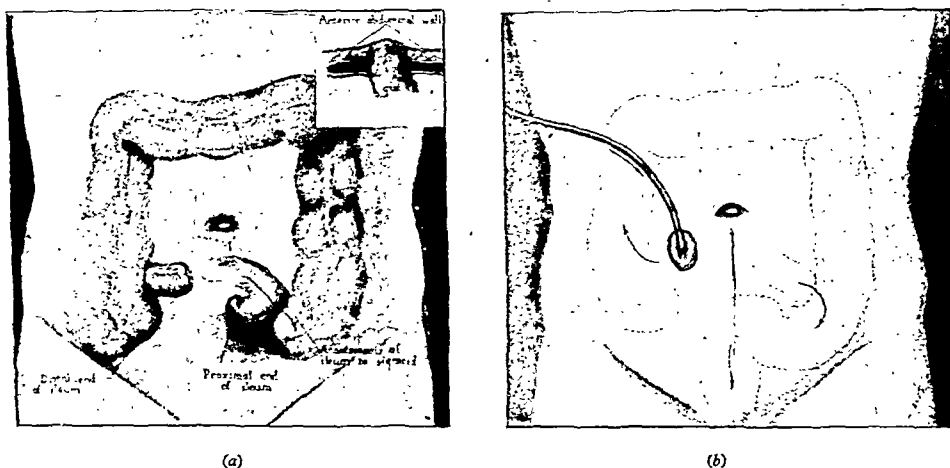


FIG. 3.—(a) Ileosigmoidostomy established after division of terminal ileum. (b) Distal ileostomy formed by opening blind end of ileum. (From Elmer R. Arn, *Ohio St. med. J.*, 1931, 27, 124-245.)

appeared to be clinical cures. The operation was followed by daily colonic irrigations through the distal end of a divided ileum, brought to the surface in right iliac fossa and this appeared to be continued for five years and longer. In one case, irrigation was discontinued and pain was felt along the course of the colon and in another case, a fistula developed which led them to carry out a colectomy. In a third case a woman was subsequently delivered of a normal infant by Caesarean section. In 1936 a case is reported from the Mayo Clinic which was not satisfactory.

On the whole this form of treatment is dangerous as a primary procedure. Anastomosis to a portion of diseased colon would appear to be wrong. Also the operation is too severe to carry out on a patient whom one pictures as being very seriously ill. It is only justifiable in an earlier stage in combination with an ileostomy as already referred to, or with a colostomy as seen in the occlusion operations. An example of the latter is described in a report in 1939 by Gaha of Tasmania. He had treated with apparent success, *eighteen* cases in eight years in the following ways (fig. 4): (a) Ileosigmoidostomy plus colostomy with occlusion of the sigmoid and ileum on either side of the anastomosis by means of two temporary ligatures of heavy salmon gut. (b) Removal of these ligatures and the placing of a third ligature round the sigmoid on the distal side of the anastomosis already established—this takes place a year later. (c) After another interval—the time not stated—the third ligature is removed and the colostomy closed. In this way the continuity of the bowel is retained and ultimately restored. It may take two years and requires three exploratory laparotomies. All the patients seem to have survived although it appears to be a very complicated method. It should be possible to produce equally good rest and bowel drainage by more simple methods.

Devine's colectomy associated with ileorectal anastomosis can also be included under this heading. In 1943 he described a colectomy in stages (fig. 5, *a* and *b*). The first stage consists of a division of the ileum 4 in. from the ileocaecal valve and also a division of the rectosigmoid ileum is approximated to rectum and a spur formed. One month

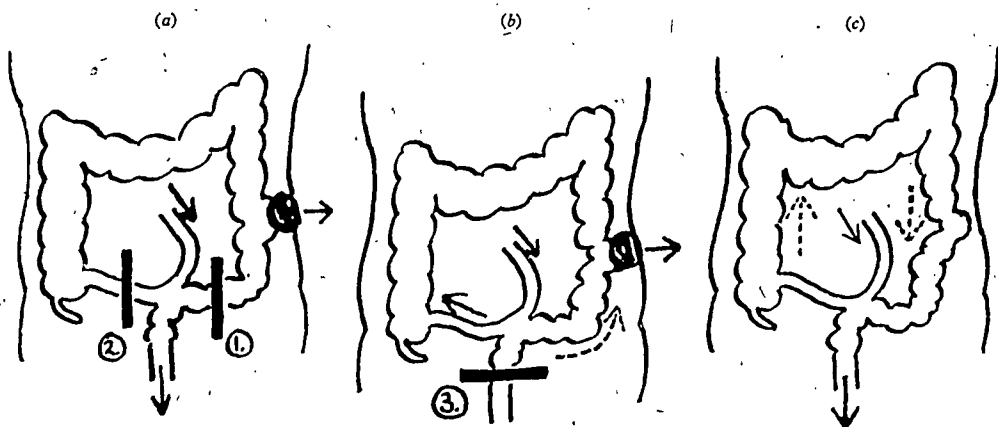


FIG. 4.—The three stages in the temporary occlusion operation described by Gaha, 1930.
1, 2, 3 = Occlusion ligatures (temporary).

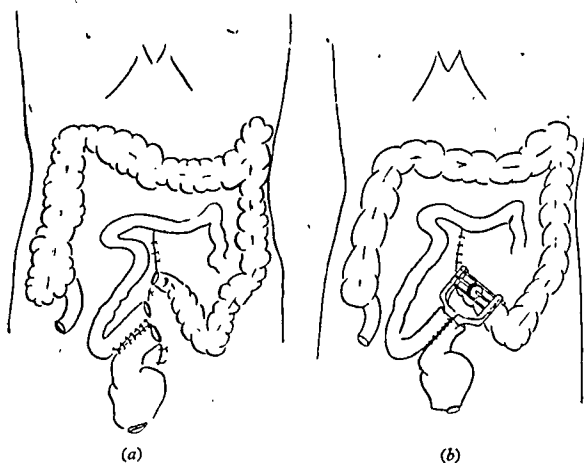
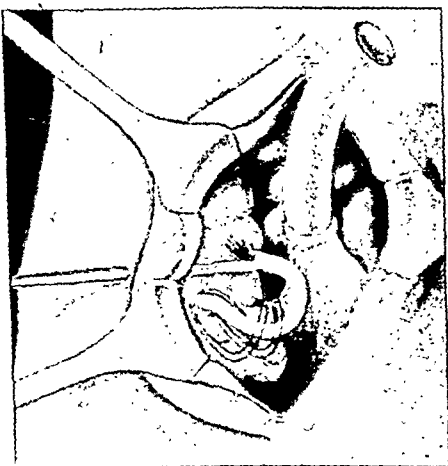


FIG. 5.—Devine's method of colectomy for ulcerative colitis. (a) Formation of the ileorectal spur. (b) Ileorectosigmoid septum crushed with an Ochsner-DeBakey spur crusher. (From Sir Hugh Devine, *Surg. Gynec. Obstet.*, 1943, 76, 137.)

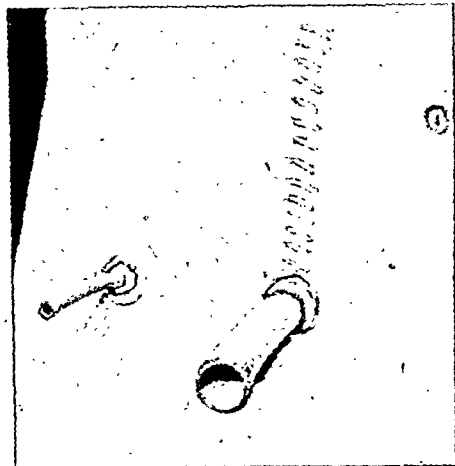
later an enterotomy is inserted to crush the spur. After two months the ileorectal anastomosis is closed. The final stage is a colectomy.

Ileostomy.—This operation consists of draining the contents of the small gut through an opening in the terminal part of the ileum near the ileocaecal valve and so putting out of action completely the whole of the colon. It is a drastic procedure and for this reason few physicians or surgeons are prepared to submit their patients to it, except after very careful consideration.

Historical.—One hundred and fifty years ago internal ileostomy was carried out as a temporary drainage of the bowel, a Witzel method or modification being used. This can only be looked upon as a temporary ileostomy, suitable for intestinal obstruction and does not have any place in the treatment of this disease. A more permanent drainage was advocated by John Young Brown in 1912 (fig. 6, *a* and *b*). In December of that year he read a paper before the Southern Surgical and Gynaecological Association of America on "The value of complete physiological rest of the large bowel in the treatment of certain ulcerative and obstructive lesions of this organ." He emphasized the importance of rest in colonic disease and referred to a parallel in the opium treatment of peritonitis, advocated by Alonzo Clarke (long since abandoned) or, the more recent so-called "Starvation treatment" of Ochsner (not yet given up and still inflicted on some patients suffering from appendicitis). Up to this time several surgical procedures had been tried,



(a)



(b)

FIG. 6.—Brown's method of complete physiological rest advocated in 1912. (a) Division of terminal ileum with insertion of tube into proximal end. Removal of appendix with tube inserted into cæcum. (b) Terminal ileostomy combined with cæcostomy. (From John Young Brown, *Surg. Gynec. Obstet.*, 1913, 16, 613.)

appendicostomy, cæcostomy, and ileosigmoidostomy. Concerning the first two, his objections were that they permitted of colonic irrigation and medication only. He brought forward another argument against these procedures by stating that, in his opinion, as fast as the colon was flushed with solution it refilled with fecal contents from the small bowel so that irrigations were of little value.

His operation was a combined cæcostomy, after removing the appendix, and terminal ileostomy after complete division of the ileum near the ileocaecal valve. His experience of this operation is based on ten cases. Three for amœbic dysentery and one for ulcerative colitis, and one for obstruction. Two were for chronic intestinal stasis and three for inoperable malignant growths of the rectum. He states that the case suffering from ulcerative colitis was in good health following the operation—no further details were given.

From this time, in the medical literature there were many references to ileostomy.

From conversation with my colleagues, I find opinions differ in regard to the degree of danger and discomfort associated with the establishment of a terminal fistula of this sort. The physiologist would lead us to believe that it would be quite impossible for us to carry on because of dehydration. This certainly is not the case for although it may be a factor in the first few days after the fistula is established, it can easily be overcome by intravenous therapy. At a later stage, the fluid contents that we associate normally with the small intestine alter in character and the discharge, within a few months, becomes solid. It is manageable before that period with a suitable container. Later, the discharge may be so firm that the box may be quite difficult to empty and clean. I think one can say that a well-established ileostomy is no worse than a colostomy—in fact, some say it is preferable. To quote Ogilvie: "There are no unheralded explosions and the discharge is *not* offensive."

Mortality.—The mortality of the operation is seen to average 30%.

This operation has brought about some dramatic results and it has been stated by many that it is the most important advance in the treatment of chronic ulcerative colitis in the last ten years. This was well shown in the first patient treated at St. Bartholomew's in 1936. Dr. Graham persuaded me to carry out an ileostomy on a young married woman of 22.

CASE I.—This patient had suffered from the disease for two years prior to ileostomy, eighteen months being spent in bed. An appendicostomy was established first—seven months after the onset—with some improvement. Her condition before the ileostomy was that she was bedridden—down to 4 st. in weight with a Hb. 5% which had been raised

from 29% by blood transfusion. Her pulse was 120/130 and temp. 99° to 100°. She was incontinent and lay on a rubber bedpan. Six weeks after the operation she was on full diet and in three months she had doubled her weight to 8 st. Following this she was able to live a normal life and has been doing war work in a factory for the last three years (fig. 7, a and b).



(a)



(b)

FIG. 7 (*Case 1*).—(a) Condition of colon nine months before ileostomy. (b) The same colon eight years after ileostomy as outlined by a barium enema.

Ideally, ileostomy is only the first step—one of exclusion—the subsequent steps being excision and finally restoration. The chances of these steps being carried out to a successful conclusion in all cases are remote when one realizes how severe must be the inflammatory reaction around and in such an ulcerated colon, and the risk one may run in subsequent removal and re-anastomosis. Also, there is the fact referred to before, that the disease starting at the distal end of the colon makes the chances of a satisfactory anastomosis of small gut to sigmoid or rectum uncertain.

In 1939 Cattell reported on 24 patients who had been submitted to complete colectomy, following ileostomy. 21 were alive—some for ten years—and the patients managed their ileostomies quite satisfactorily and they appeared to be active and in good health.

On the other hand, if an ileostomy is decided upon early in the disease, it may be possible to close the fistula and restore the continuity of the ileum. This was advocated by Cattell three years later. Out of 9 cases, 5 yielded favourable results. Success of this procedure will depend upon (1) an appreciable period—say six to eight months—free of a clinical return of symptoms; (2) sigmoidoscopic appearance showing the inflammatory processes to have healed or be inactive; (3) a colon which can be distended with some evidence of haustral-markings after evacuation of a barium enema. Maingot also reported, in 1942, a successful case of restoration following ileostomy established a year previously.

When a terminal ileostomy is decided upon the patient must be made to realize that in all probability this condition will remain for the rest of his or her life and that it is only the exceptional case which will allow of the continuity of the bowel being restored with or without a colectomy.

Types of Ileostomy, Temporary and Permanent

Of the permanent type there are two varieties: (1) "Terminal" or single-barrel. (2) "Loop" or double-barrel.

A "terminal" ileostomy is established by the division of the ileum at four to six inches from the ileocaecal valve and bringing out the proximal end as a fistula. The distal end is closed and dropped back into the right iliac fossa (figs 8, *a* and *b*).

A "loop" ileostomy is where a "loop" of terminal ileum is brought to the surface of the abdominal wall and supported either by a rod—as is the case in a colostomy—or, more usually, divided so as to form two separate openings on the surface (fig. 8, *c*).

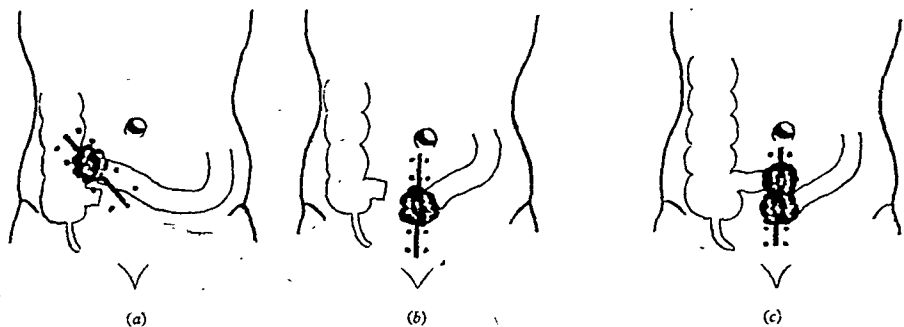


FIG. 8.—Types of external ileostomy: (*a*) and (*b*) "Terminal" or single-barrel. (*c*) "Loop" or double-barrel.

This type of ileostomy is advised in the severe fulminating type as it is quicker and less hazardous to perform.

Sometimes these openings are brought out through different incisions: the proximal opening will act as an artificial anus and the distal opening may serve as a means of applying any form of medicinal treatment required to the diseased colon (figs. 9, *a* and *b*).

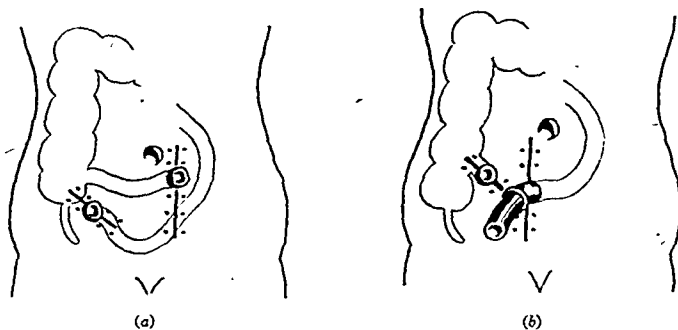


FIG. 9.—Types of ileostomies—double-barrel; (*a*) After Cave and Nickell. (*b*) After Cattell.

A further use of this distal opening has been advocated by Hurst and Harvey-Stone of Baltimore. The former suggested its use for the re-education of the colon prior to restoring the continuity of the small intestine. He advocated a reinjection of the faeces discharged from the ileum through the proximal ileostomy opening into the distal and noting the effect. When this can be carried out without any severe reaction to the patient, then he considered that a closure could be effected. The latter used the distal opening for injecting the colon with two litres of normal saline and examining the fluid after retention for some time. If no red blood cells or white blood cells were found, he considered the bowel safe for closure. This is ingenious and has been carried out by some surgeons in this country (Maingot, Gaymer Jones and McNeill Love).

Unless the inflammation of the rectum and colon is arrested early in the disease, the changes resulting are so extensive that the mucous membrane is destroyed, the muscular walls are fibrosed and the function of the bowel can never be restored satisfactorily.

Complications of Ileostomy

The operation of ileostomy is sometimes followed by complications, apart from those associated with the disease.

(1) *Prolapse of the ileum*.—This is the most common complication in the Mayo Clinic report and five patients died as a result of it—four from operative interference to overcome the prolapse. A mild degree was seen in one of our series and was successfully treated by injections of phenol in almond oil. Gabriel has noted it in two of his five cases. A possible factor producing this complication is the form of bag or box worn after the operation. Fig. 10 shows the bag advocated by Barger and used in the United States. My feeling is that this type of cup may be held partly responsible, and I base this on our experience in the management of colostomies. We have all seen the ill-effect of a cup over a colostomy. It acts like a suction bell. It produces prolapse of the mucous membrane, or even the whole bowel wall. The desire of the patient for such an apparently safe device should be discouraged. The box has gone through many phases in development in our hands.

With the co-operation of the instrument-maker, Mr. Donald Rose, we have got adequate containers which are not bulky and are now "stream-lined" (figs. 11, *a* and *b*).

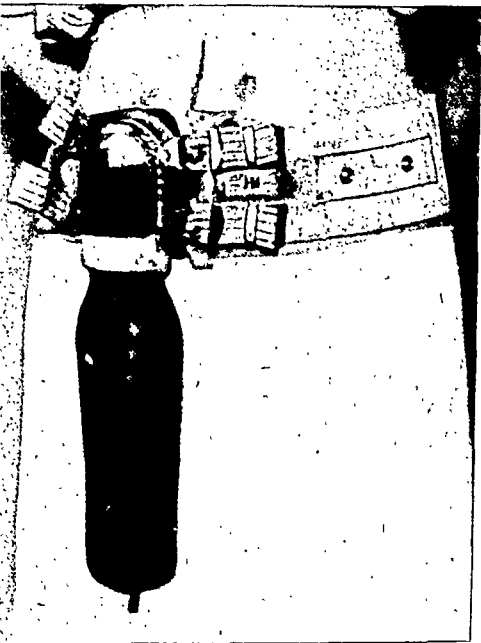


FIG. 10.

FIG. 10.—Ileostomy bag as advocated by Barger. (From John Arnold Barger, "The Modern Management of Colitis", p. 98, published by C. C. Thomas, Springfield and Baltimore, 1943.)

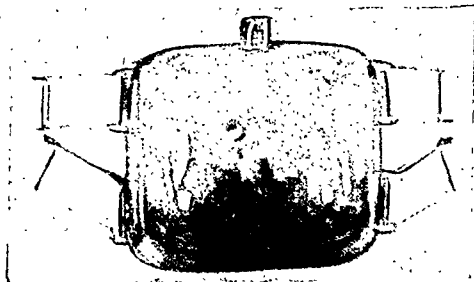


FIG. 11a.

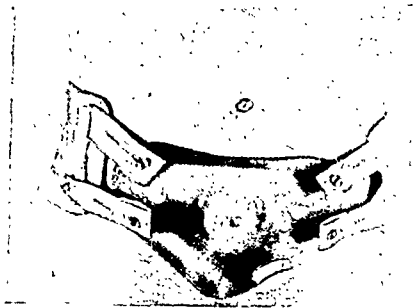


FIG. 11b.

FIG. 11.—(*a*) Ileostomy box fitted over medial ileostomy (Case I). (*b*) Another type of box fitted with Outlet (at patient's request) (Case II). (Note scars of subphrenic abscesses R. and L.)

(2) *Formation of abscesses and fistula*.—This usually occurred between the ileum proximal to the stoma and adjacent structures including the abdominal wall, as a result of a perforation. In some cases involvement of the distal ileum by the spread of disease may be the predisposing factor that leads to the abscess or fistula. Perforation of the ileum following late ileostomy has been referred to recently by Crandon, Kinney and Walker of Boston. They report two cases which resulted in peritonitis and death. As a result they suggest that the ileostomy be performed at least 90 cm. above the ileocaecal valve—assuming I think an extension of the disease from the colon along the ileum before ileostomy is carried out. One patient in our series died from this complication, and another perforated the ileum just proximal to stoma, which resulted in a right anterior and posterior and a left anterior, subphrenic abscess from which he recovered. This is not referred to by the observers, but it has occurred also in a patient of Sir Philip Manson-Bahr's, whom I was privileged to see in 1936 before I did my first case. He died last year of a subphrenic abscess—nine to ten years after the ileostomy.

The details of this case were as follows:

CASE II.—Male, aged 21.

Six years before, onset of diarrhœa. Treated medically (fig. 12, a), until he developed a vesicocolic fistula with stricture of the rectum 4 in. up. Weight 6 st. Terminal ileostomy through right gridiron incision. Put on 4 st. in two months. Urinary infection cleared within three months. Well until one year and eight months when he complained of abdominal pain and vomiting. Subphrenic abscess found and drained posteriorly (14 oz. pus) (fig. 12, b). Three months later I set out to do a colectomy, 1st stage,



(a)



(b)

FIG. 12 (Case II).—(a) Appearance of colon three years before formation of vesicocolic fistula. (b) Barium enema four years after terminal ileostomy showing track in right iliac fossa leading to a subphrenic abscess cavity.

but found and drained a right anterior subphrenic abscess. A month later a left anterior was drained. He returned to hospital two months later on account of a fæcal fistula from the right subcostal wound. Skiagrams showed this to come from the ileum, not colon. Reformed ileostomy 6 in. from original stoma through a right paramedian incision closing the original fistula.

(3) *Intestinal obstruction* is serious, and five out of thirteen of the Mayo series died from the subsequent operative interference to overcome the obstruction. It may be in the form of an acute ileus or a temporary block soon after the fistula is established.

I found that temporary and recurrent signs of intestinal obstruction not infrequently occur within the first ten days following operation. This is very alarming to the surgeon, and disappointing to the patient. It can usually be overcome by inserting a soft, red rubber catheter into the fistula so as to extend well into the abdominal cavity. It is best not to leave the catheter in the lumen on account of possible irritation which may lead to adhesions round the ileum and may account for abscess formation subsequently.

PERSONAL OBSERVATIONS ON ILEOSTOMY

I would like to refer to eleven patients treated at St. Bartholomew's Hospital by ileostomy since 1936, and to certain difficulties arising in connexion with this operation and to the lessons learned from these cases. Four died within six months (36% mortality). Of the remaining seven, six are alive and well four to eight years after the operation. One died within a year from a perforation leading to peritonitis.

Good results from surgical treatment depend not only on the care of operative details but also on the pre- and post-operative management. The latter implies close co-operation between physician and surgeon.

Pre-operative care.—The outstanding point is to overcome deficiencies which are associated with this disease in its severe forms. These may be grouped under the following headings: (1) *Vitamin deficiency*: This is very liable to occur owing to the most serious upset of the gastro-intestinal tract. Some vitamins are best administered by the intramuscular route, when the patient can be brought to saturation point with certainty before the operation. (2) *Anæmia*: This is always most marked and repeated blood transfusions are of the greatest value. In the milder forms of the disease this treatment alone has produced great improvement: (3) *Disturbance of mineral metabolism*. (4) *General malnutrition and inanition*.

OPERATION

All our cases had gas-oxygen anæsthesia and there seems no contra-indication to this. Local anæsthesia can be used if desired as the operation is usually a limited one in the first stage of the disease.

Incision.—There are two alternatives (1) Mid-line or right paramedian. (2) Gridiron, in the right iliac fossa. The former will have to be used when a previous appendicostomy or cæcostomy has been done, and this is closed later under local anæsthesia.

The gridiron would appear to be the more satisfactory when the abdominal wall is intact, but it must be placed as near the rectus sheath as possible, in order to fit the box comfortably over it. It also allows an easier exploratory laparotomy if colectomy is undertaken later. Bringing the ileum out too near the mid-line increases the risk of intraperitoneal complications later. On opening the peritoneum, no handling of the diseased colon should be done and the terminal ileum should be identified by the fold of Treves and brought to the surface.

If a terminal ileostomy is decided upon, the next step is to divide the ileum about 4 in. to 6 in. from the ileocecal valve or more remotely if any signs of disease are present. The distal end is closed, and dropped back into the iliac fossa. The proximal end is maintained outside the abdominal wall by dissecting back the mesentery, to allow of an inch and a half at least of the bowel to project beyond the surface. The mesentery should be fixed to the peritoneum at the upper end of the incision to avoid prolapse (fig. 13).

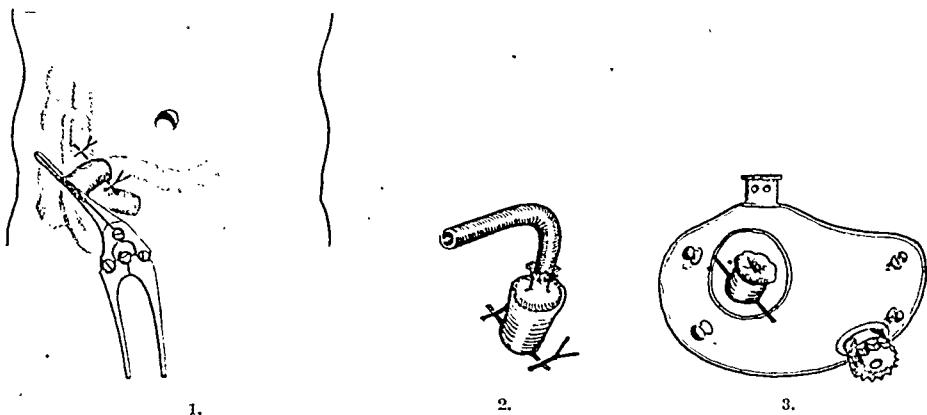


FIG. 13.—Formation of a terminal ileostomy through a gridiron incision. (1) Peyer's clamp left on proximal end. (2) Insertion of a Winsbury-White tube after removal of clamp. (3) Application of temporary box.

Post-operative care.—I leave the proximal end clamped for twelve to forty-eight hours if possible. The crushing clamp is then removed and replaced by a Winsbury-White tube inserted into the lumen of the projecting gut, and held by a purse-string suture. This will give the incision a chance to heal—an important factor in the subsequent comfort of the patient. If the contents of the small intestine contaminate the wound it will break down and the skin will get very sore. As a first dressing, vaseline gauze can be applied around the projecting bowel and is comfortable. When the tube is inserted the skin is given a liberal coating of aluminium paste. This consists of powdered aluminium 10 parts, and zinc oxide 90 parts.

Another important point in my opinion is to fix a temporary box immediately the tube is removed and the fistula is working. This, I am convinced, limits the trouble in connexion with the skin. Applications such as collodion, latex or tincture of benzoin and other recommended applications, have been, in our hands, a danger rather than a help, in the preservation of the skin around the fistula.

Another small point is the taking of Reduced Iron (*ferrum redactum*). One of my patients is quite convinced that the skin around the ileostomy is kept in perfect condition by taking enough to cover a sixpence after each meal.

There appears to be only one real disadvantage to a terminal ileostomy, and that is when a stricture develops in the colon. This would give rise to a blind loop of colon, which cannot be drained effectively. Fortunately, stricture formation in the colon after ileostomy is extremely rare, but if it does occur, colectomy is indicated.

Colectomy.—There is no doubt that when one realizes the complications of the disease that may follow in spite of ileostomy, there is a place for colectomy in the later stages of treatment. Two factors that may have limited this further stage—that of excision—are: (1) The high operative risk. (2) The sufficient relief and subsequent improvement in health following the ileostomy alone, which makes subsequent colectomy seem inadvisable.

Colectomy associated with ileosigmoidostomy seems to be unsound, as this would not prevent the development of complications which are known to occur around the rectum and anus, and which may be so serious for the patient.

Colectomy associated with ileostomy is a sound procedure, and the indications for this seem to be: (a) In patients who continue to get a lot of discharge from the rectum with consequent invalidism. (b) In patients who develop stricture formation in the colon. (c) In patients who continue to suffer from complications of the disease, such as arthritis. One patient in the Mayo group obtained complete relief from arthritis, suffered for nine years.

Carcinomata are known to arise in a bowel previously affected by ulcerative colitis in about 3% of cases and under these conditions it is wise to resect the bowel completely. I carried out a limited resection in a patient with a long-standing ulcerative colitis who developed a carcinoma in the colon. Following the excision I left a temporary colostomy hoping to improve the condition of the large bowel on the distal side. I then closed the colostomy after temporary improvement with sulphonamides. The patient died from the original disease within a year.

I feel that this type of case would have been better treated with an ileostomy and complete colectomy. The ileostomy would have been a small price to pay for his life. From the Mayo figures, 7 out of 18 patients alive and well fifteen years after an ileostomy had had a colectomy.

CONCLUSIONS

(1) The treatment of chronic ulcerative colitis must be based on accurate diagnosis. (2) Adequate and complete medical treatment must be persevered with before any form of surgery is undertaken. (3) The indications for surgical treatment are confined to a small group—approximately 15%. In those patients (a) where the disease is progressive and endangers life in spite of adequate medical treatment; (b) who show relapses or recurrences following an initial course of successful medical treatment; (c) who develop complications associated with the disease; (d) in some patients (never children) who have a severe fulminating type of disease. (4) Early operation is not justifiable in this disease, as a rule. (5) The type of operation that will give the best results in the majority of patients depends on the production of absolute rest to the diseased colon. This is best effected by means of an ileostomy. The response to ileostomy in the immediate post-operative period is remarkably good. (6) Ileostomy appears to be more efficient in arresting the disease than appendicostomy, cæcostomy or colostomy. Irrigation of the bowel appears to be of no great value and has fallen into disrepute. The value of the sulphonamides has not been proved. (7) In a small proportion of cases, an ileostomy is associated with complications. If these develop, or the signs of the disease in the colon persist, it is wise to proceed to colectomy. (8) Ileosigmoidostomy is dangerous and uncertain in its results and depends entirely on the condition of the sigmoid and rectal wall—though ideal from the patient's point of view. (9) "Once an ileostomy, always an ileostomy" is the safest dictum for the majority and to quote Cattell: "An ileostomy is the price that some patients must pay for life."

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Section of Laryngology

President—C. GILL-CAREY, F.R.C.S.Ed.

[December 1, 1944]

CAUSES OF FAILURE IN THE SURGICAL TREATMENT OF CHRONIC FRONTAL SINUSITIS

H. G. Bedford Russell: I wonder how many of us could face with equanimity a parade of all our operated cases of chronic frontal sinusitis. When we meet with an acute mastoiditis we operate, and we find that in a proportion of cases every cell contains oedematous membrane and no pus, but we do not on that account think that we have operated unnecessarily, and Wilde's incision is a recognition of the importance of relieving pressure. In many cases of frontal inflammation the symptoms subside, and we have a virtuous feeling at having avoided an unnecessary operation. But if the pressure has been maintained too long, the infection merely crouches for another spring when the next upper respiratory tract infection comes along; and so on till one day the pressure can no longer subside.

If the skiagrams show haziness some months after the symptoms have subsided, chronic frontal sinusitis is already in being, as in the case of a boy of 15 who last April had right frontal pain with prolonged deafness and toxæmia. No pus was visible. Skiagrams showed the frontal sinus was hazy and the antrum was seen to contain polypoid mucosa. The antrum was exenterated, after which the deafness and toxæmia suddenly improved; and in a recent skiagram the frontal haziness has disappeared. If it had not, surgery would have to be considered, as treatment now is far easier and better than if it were left till complete sinus-block occurred a few years later.

For many years it has been the fashionable thing to temporize with frontal sinusitis: the first step will be a submucous resection, or a reduction of the middle turbinate. Then perhaps drainage of an ethmoidal cell or palliative treatment of the antrum. I have even seen one case in which the rake's progress included submucous resection of the septum, then no less than forty antral lavages, followed by a Caldwell-Luc operation. And it often happens that there is a gratifying relief of symptoms after each step. But the symptoms may recur, and the diagnosis has to be made sooner or later; and the later it is the worse for the surgeon as well as the patient. By this time the tissues in the infundibular region are thoroughly soaked in streptococcal juices, and the bone has been somewhat thickened by the previous operative work in the neighbourhood. Then, if the local structural considerations permit, intranasal drainage is undertaken: and there is no doubt that a percentage of cases do well for a number of years after it, with the help of local manipulations of sorts.

Howarth has given clear indications as to the type of case suitable for an intranasal approach (*J. Laryng.*, 1931, 46, 397).

Finally the case comes to exenteration, the success of which is prejudiced by the deterioration in local and general health which has inevitably occurred. All of which is to say that I advocate much earlier diagnosis, and open operation upon the frontal as a first step, instead of as an appendix to multiple palliative operations.

A common cause of failure is regarding the frontal sinus as an isolated offender. I regard sinusitis as originating in the diffuse inflammatory processes associated with the exanthemata, influenza, pneumonia and the like. The sinusitis is usually catarrhal at the outset, and yields to suitable palliative treatment. If children's sinuses are examined after convalescence from such illnesses, there is clinical and radiological evidence of sinusitis in a percentage of them. I recall one case following measles in a child of 10, in which the frontal sinuses were found crammed with inflamed polypi, and there was already a frontal lobe abscess; but as there was no pus in the nose, it had been thought that he could not have sinusitis.

The diagnosis of sinusitis does not depend upon the presence of visible pus, for the tissues respond to streptococcal invasion by the production of œdema rather than pus. I have had cultures made in many cases from the submucosa of the frontal after sterilization of the surface of the membrane, and found a copious growth of pathogenic organisms in cases where no pus has been seen clinically. It is even possible to grow bacteria from the deeper layers of biopsies from the mucosa near the ostia of the sinuses—a diagnostic procedure of definite clinical value. It is important in frontal sinus cases to have anaerobic cultures: the infection in frontal osteomyelitis is an anaerobe. In one case, anaerobic cultures from the interior of a polypus grew a staphylococcus, which did not come up till the fifth day.

In cases of catarrhal inflammation which do not receive suitable palliative treatment the infection may persist after the symptoms have disappeared, to recur with increasing local damage, with or without pus, with further upper respiratory infections until the swelling happens to force recognition by the occurrence of sinus-block. So that the behaviour of a sinus in response to operative treatment is conditioned by previous tissue damage, and cut he never so wisely, the surgeon's results are, to some extent, determined by matters outside his control.

This view calls for recognition of catarrhal frontal sinusitis while the local changes are reversible, and the immediate institution of suitable palliative treatment.

Failures due to technical imperfections are largely the result of fear of damaging the appearance or the function of neighbouring organs or of causing osteomyelitis by opening up cancellous bone. The few cases of osteomyelitis I have seen have quite certainly occurred owing to a *lack* of wide exposure. A case was recently seen in which an external operation had been done through a small incision, which had failed to disclose the existence of imprisoned œdema. I have not seen osteomyelitis follow the complete removal of infected mucosa, with the ventilation which can only be achieved by a free exposure.

Cosmetic failure has been less in my cases since the avoidance of delay entailed by multiple palliative operations. On the assumption that the origin of the frontal trouble must have been a diffuse affair, an increasing number of cases have been treated by exenteration of all the sinuses upon one side at the same time.

A median incision has been employed in over forty cases during the last six years and has been found to give satisfactory access, especially if both sides have to be examined simultaneously.

Diplopia, even of temporary duration, seems less likely to occur with wide elevation of a sheet of periosteum including the origin of the superior oblique pulley rendered possible by this approach.

Exenteration has heretofore not commended itself in the case of young subjects owing to the resulting disfigurement; but recent work by plastic surgeons offers reasonable hope that this difficulty may be overcome after a suitable interval by the introduction of fresh cancellous bone chips to restore the lost contour. Mowlem has successfully employed such grafts for restoring defects in the cranium, the mandible and the long bones, so that the method should be applicable even to large sinuses approximating to the external angular process. Osseous union with the underlying frontal remnants will obviously be desirable, and though it may be necessary to roughen any very dense cortical bone to ensure this, simple removal of the overlying layer of scar is usually sufficient. Experience will show how soon after exenteration it should be safe to insert the bone chips. With the help of penicillin and chemotherapy it might be possible in suitable cases to avoid the long wait that has seemed prudent hitherto. I report two successful cases, one of two years' standing and one of six weeks'.

Recurrence of attacks after exenteration has occurred in some of my cases, and has been invariably associated with an upgrowth of mucosa from the nose in an attempt to reline the cavity from which one had so carefully removed it. This "colonizing"

habit of the mucosa is of service in the other sinuses, but in the case of the frontal the upgrowth tends to get nipped by scar-tissue in the region of the infundibulum owing to the removal of bone which is occasioned by most operative procedures with an external approach. During the last two years in an attempt to checkmate this colonizing habit, the infundibular mucosa has been invaginated into the nose and allowed to hang down as a polypus, while the wound above has been packed, its pedicle being severed a few weeks later. Cases have been observed for two years after this procedure without evidence of upgrowth of mucosa.

Skin-grafting by Ferris Smith's method was tried in several cases from 1935 onwards, and the opinion was formed that this method is not the complete solution of difficulties. The behaviour of grafts is variable. There is a tendency for the skin-graft to proliferate. Out of ten cases so treated in that year, recurrence of symptoms has necessitated reopening of the sinus in three cases. In one case the frontal sinus cavity was found occupied by a sort of cholesteatoma. In another the nasal mucosa was found to have re-lined most of the cavity. In another case there was invasion of part of the nasal cavity by a skin-graft implanted in the frontal sinus. The suggestion is made that success in skin-grafting operations depends on the fact that the skin-graft prevents invasion by mucous membrane, so permitting scar-tissue to fill the cavity. In one case of exenteration in which the wound was left open and packed for several months, there followed an ingrowth of squamous epithelium which reached as far back as the posterior ethmoids, causing crusting. It completely disappeared in about four years.

In conclusion, I am in favour of wider recognition and palliative treatment of the catarrhal stage, which will often prevent the need for operation years later. If operation becomes imperative, it should usually consist of open operation and exenteration at the outset with avoidance of the usual series of palliative operations.

Tantalum Implants for Skull Defects

Lieut.-Colonel Norton Canfield, U.S.A.M.C.: The frontal sinus has ever been one of the most difficult regions for the rhinologist. Head pains or headache is so frequent that when it occurs the patient refers to it himself as his "sinus" or his "sinus headache". The frontal sinus must always be considered with such a complaint and to establish it as a definite ætiologic factor for the pain has taxed the ingenuity of our most intensive diagnostic methods. Even when infection exists in the frontal sinuses it may not be the cause of the symptoms. Hence patients with diseased sinuses are often treated by operation and receive no relief from the pain. Because of many failures to relieve pain which was thought to be due to diseased frontal sinus, I have come to believe that pain does not emanate from chronic frontal sinus infection without increased intrasinus pressure. To demonstrate this pressure, a combination of intranasal and X-ray examinations, and at times an actual trephine of the sinus wall may be needed to give us the necessary evidence.

Having decided that the sinus must be opened, and portions of its bony wall removed to effect a cure, we have constantly before us the consideration of the post-operative cosmetic appearance of the patient. Failure to remove the infection at the first operation causes delayed healing of the wound. Excessive removal of bone causes disfiguring contours. Various methods have been designed to eradicate the disease and leave the patient happy about his scars. Methods of plastic revision of the contours by living tissue and foreign bodies have both been tried, but even so, the ideal and certain method has not yet been devised.

As I mentioned at the meeting last May (*Proc. R. Soc. Med.*, 1944, 37, 674), the element tantalum is in many ways ideal for cosmetic restoration about the head.

Major John Kane will report some actual cases of injury involving the frontal sinus for which tantalum has been employed.

Lieut.-Colonel R. G. Spurling (*Senior Consultant in Neurosurgery, U.S.A.M.C.*), who showed a film of the technique of plastic repair, said that the film had been made for the instruction of neurosurgeons in the Army so that they could better restore the deformities caused by war wounds. The application of the method to the whole problem of restoration after sinus operations was Colonel Canfield's idea. Many of these war wounds had involved the frontal sinus and the base of the nose, and with tantalum it had been possible to obtain satisfactory cosmetic results. His personal experience of tantalum extended back only for two and a half years, but the first cases

were reported four and a half years ago; so far as was known the results had stood up to the passage of time, and tantalum had proved to be a perfectly inert material for burying in the tissues.

The film was then projected. It illustrated one-stage and two-stage procedures as carried out at the Walter Reed General Hospital, Washington. Tantalum plates of a thickness of 15/1,000 in. were ideal for cranioplasty. The film began by showing the impression being taken on dental compound of the skull defect and then the various stages of the plastic operation.

Several of the cases had been reported from various clinics to have developed infection after the plate was inserted—in other words, soft tissue infection—and this had been treated successfully without disturbing the plate. In fact, at one of their hospitals the medical officer in charge had drained the brain abscess through a hole he had made in the tantalum plate, without disturbing the position of the plate in the least, and that patient had remained well during a period of three months' observation before returning to the United States. Therefore he thought that this tantalum element was a very important adjunct to surgery.

Major John Kane, U.S.A.M.C., then read his paper describing the use of tantalum in some cases of injury involving the frontal sinus.

The President said that two main points for discussion arose from the papers, the choice of the type of operation according to the pathological conditions present, and the merits of obliteration of the frontal sinus by tantalum implants or bone chips. Personally, he felt that, whenever possible, the bony walls and mucous membrane of the ostium should be preserved. To avoid chronicity and more extensive operations, he was in favour of temporary drainage by means of a small opening in the floor of the sinus in subacute and early chronic cases.

Walter Howarth : Some twenty years ago I said that in my opinion the ethmoid was the key to the frontal sinus, and in the intervening years I have not seen any reason to modify that opinion. This being so, it follows to my mind that the reason why some cases of chronic frontal sinusitis do not get well after operation is because the ethmoid has not been dealt with adequately and so reinfection or recurrent infection occurs from below.

There was one specimen in the Onodi collection, No. 93.1 (illustrated in the catalogue which Mr. Layton drew up for the Royal College of Surgeons), which illustrates my meaning, as it shows a remarkable development of the labyrinth. Here is a large sinus extending laterally almost to the temporal fossa and expanding the roof of the orbit backwards towards the lesser wing of the sphenoid. The fronto-nasal duct is distorted to a chink by two encroaching anterior ethmoidal cells, and the posterior one of these has an orbital process, an orbito-ethmoidal cell. There are abnormal cells of the bulla group and others in most unusual situations. It is enough to fill one with despair should one have to deal surgically with infection in such a maze. Fortunately, however, the majority of ethmoids are much simpler, though—like fingerprints—no two are exactly alike.

Exposure of the nasal end of the fronto-nasal duct by the high resection of the anterior end of the middle turbinate is a procedure of the greatest value which undoubtedly can produce resolution in a certain number of cases of not too long duration; but in the majority of cases simple drainage is not enough, and we must prevent reinfection. For this reason, I like to exenterate the anterior ethmoidal cells, and to do this I employ the method designed by Mosher. This begins by breaking into the cell of the agger nasi and then going backward external to the line of attachment of the middle turbinate. By this means, it is easy to clear any cells that encroach on the fronto-nasal duct and floor of the frontal sinus. All that is then necessary is to pass a series of solid metal sounds up into the sinus. No rasping or cutting in the region of the bony ring that guards the sinus should be attempted. This is unnecessary, and it will be found that the sinus now drains freely. I do not like washing out, and content myself with the passage of sounds and occasionally pass a silver wire tipped with solid silver nitrate to reduce any exuberant granulations or swollen mucosa in the neighbourhood of the ostium.

A good many of the cases referred to me have had several previous operations and some have had fistulous tracks. In these, and in cases that have not yielded completely to the intranasal operation, an external approach is advisable. I still think that the incision and method that I have long advocated give the best exposure. I have

given the transantral, infra-orbital and other routes a good trial, but I am unable to get a satisfactory exposure of the anterior ethmoidal region and the fronto-nasal duct. I like to see what I am doing, and particularly do I like to see the posterior wall of the sinus and its lateral extensions.

When we open these sinuses it is often obvious that the reason for the failure of the intranasal and other operations is that an infected ethmoid is the cause. Naturally there is a limit to what can safely be removed by intranasal means. If the infected ethmoid is removed and free drainage assured, making a very large fronto-nasal duct by removing the nasal process of the frontal bone and the ascending process of the superior maxilla and skin-grafting this, the large majority of cases get well.

Why, in some cases, does this operation fail, and why, in others, is it an unsuitable procedure? (1) It may fail because the drainage and ventilation through the new fronto-nasal duct are not adequate. This is by far the commonest reason and is usually the fault of the surgeon. (2) It may fail when the sinus is loculated, as I well remember in one case in which later there was found to be a large loculus in the temporal region, communicating with the main sinus by a very small opening. (3) It may fail because the other sinus is infected and communicating by a hole in the intersinus septum. On several occasions, by enlarging this hole, I have drained the two sinuses into the one side. (4) It may fail because behind the sinus there is a leaking frontal lobe abscess. I have had three cases of this nature, and they may be very difficult. It is a possibility that should be borne in mind, and that is why I like to see the posterior wall of the sinus.

In what cases is a drainage operation unsuitable? One sometimes comes across long-standing cases in which there is high-grade degeneration of the mucous membrane, denuded bone, necrotic areas and fistulous tracks. Such cases are to my mind only amenable to an obliterating operation, and by far the most satisfactory of these is Riedel's. Fortunately, the cases requiring this procedure form a very small percentage. The resulting deformity is severe, but this should not influence one's judgment. In the excellent film shown by Colonel Spurling and the admirable results obtained by Colonel Canfield and Major Kane, we have seen how wonderfully the cosmetic aspect can be improved, and I am always lost in admiration at the results achieved by my colleague Professor Kilner in my own cases that require plastic surgery. It is certainly an additional comfort to be able to adopt the right surgical procedure without a qualm.

Norman Patterson said that in his opinion the large majority of cases of suppuration in the frontal sinus recovered without any surgical interference at all. He agreed with Mr. Howarth that the ethmoid was the key to the whole situation because polypi or inflammation in this region interfered with drainage. Cases of frontal sinus suppuration might be divided into three groups. The first group consisted of those in which there was little change in the mucous membrane lining the sinus. Most of those cases would get well by non-surgical treatment, aided, when necessary, by chemotherapy. There were other cases in which the mucous membrane was diseased, often associated with polypoid masses interfering with drainage, which might come within the realm of surgery. There was a third class where the bony walls were diseased; possibly a fistula was present which opened on the surface. Orbital or intracranial extensions might occur without any obvious defect in the bone. He had encountered a case where there was a subperiosteal abscess, a frontal sinus abscess, and an epidural abscess, without any gross involvement of the bone. The infection, however, had percolated forwards through the anterior wall and backwards through the posterior wall. The class of case in which these conditions were present—obvious disease of the mucous membrane or bony walls—should be treated by fairly extensive operation. Each case must be judged on its merits. The operation he advocated in cases where frontal sinus disease was associated with gross changes in the ethmoid, was one which made a complete exposure possible; he intended to describe his method at another meeting. It was quite impossible to deal adequately with the ethmoidal galleries, especially if they are packed with polypi, by any intranasal method.

He had seen only one case of osteomyelitis associated with an operation for frontal sinusitis. This was a patient sent to him from the East; after nine operations, including the removal of nearly the whole of the frontal bone, he recovered. He had seen three cases of osteomyelitis, all fatal, following operations on the antrum of Highmore.

With regard to incisions, he thought the best incision was just underneath the hairy eyebrow. He considered a median incision disfiguring and quite unnecessary. As far as diplopia was concerned, a permanent diplopia seldom occurred. Practically

the only operation which he performed on the frontal sinus, if the case did not clear up by drainage, involved complete removal of the anterior wall and floor. This left a certain amount of deformity which could be remedied later by employing a fat graft; the employment of tantalum might offer a solution of this problem.

V. E. Negus said that he had had a great deal of trouble with chronic frontal sinusitis during the whole of his professional career, and particularly during the war.

In acute fulminating frontal sinusitis, from practical experience he thought the solution would lie in the treatment of the maxillary sinus by lavage, together with penicillin.

In chronic frontal sinusitis he took it that they were all agreed, with the possible exception of Mr. Bedford Russell, that everything possible should be done inside the nose first before any external operation was attempted. He had strong views about that; for example he saw a certain number of cases which had failed because the septum had not been put straight. It was impossible to expect the frontal sinus to show a satisfactory recovery if the nasal fossa on that side were much obstructed. Sometimes the maxillary sinuses or ethmoidal cells had not been dealt with properly. He would therefore make every effort to cure the patient's frontal sinusitis by intranasal treatment. He did not subscribe to the opinion that the patient must not be submitted to a second operation and that the first operation must be so thorough that the patient would not require another. He saw no objection to a second operation if this were necessary. He would reserve the external operation for cases which had failed with simpler measures.

When the patient was still left with headache and discharge due to frontal sinusitis, then an external operation was advisable. Intranasal operations to enlarge the fronto-nasal duct did not appear to be satisfactory. If the patient had received all the treatment which could be carried out inside the nose without alleviation, what should then be done? One view was that sinuses should be looked upon as unnecessary, superfluous, without function, and should therefore be destroyed. The other was that an attempt should be made to restore them to their natural condition. He took the latter view. In the frontal sinus he attempted to give free ventilation and drainage by making a new and larger fronto-nasal duct without destroying or interfering with the sinus itself.

To obliterate the sinus was very difficult. Often there were pockets left which formed recurrent abscesses; he had had to reopen in these cases, lift up the skin, and put in a sac-like skin-graft. Should the lining of the sinus be removed? He thought it should not be, thus accepting the original recommendation of Howarth. The procedure seemed to be unnecessary, and a number of cases got pocketing afterwards. He had had to operate on some of the failures.

He could not see the object of the mid-line incision. It seemed to be going further away from the area one wished to approach. It was not necessary to remove the rest of the floor of the frontal sinus as was done in the original Howarth operations, but they were greatly indebted for other details of the operation. Through the opening made it was possible to get a clear view of the base of the skull, and the ethmoidal cells could be removed if they had not already been cleared intranasally, which was a difficult procedure. He did not believe that more should be done than was required, or more ciliated epithelium removed than was absolutely necessary.

Following up his fronto-ethmoidal operation, he put in a tube and a skin-graft, which should not be too large, packing, if necessary, with a small piece of ribbon gauze covered with oiled silk. After removal of the tube ten days later there should be no necessity for after-treatment, and it should be possible to pass a cannula or sound easily into the frontal sinus.

He had collected the records of 100 patients on whom he had operated by the external route. Practically all of them had had everything done inside the nose that could be done, and sometimes rather more than seemed to be desirable. He had divided the cases into two groups, pre- and post-1932, that being the year in which he had started to put in a skin-graft in every case. Of the 31 earlier cases 10 were cured and 14 were unsuccessful. By "cured" he meant that they had no symptoms and the cosmetic result was good. Of the 14 unsuccessful cases 4 had later a grafting operation with a successful result, and 8 an obliteration operation. Seven were untraced. Of the 75 later cases, 20 of whom had undergone previous external operations elsewhere; there had been good results in 56 (the patient had been freed from headache and discharge);

of the remainder 12 were untraced, and 2 were of such recent date that it was unfair to include them. The bad results numbered 7; of these 2 had to have a second graft, and 3 had obliteration afterwards. One of these cases was a neurotic individual, who committed suicide afterwards. Two others died after operation. One case had skin-grafting by someone else previously and later developed an orbital abscess which was treated by an ophthalmic surgeon. He included it only because he did an external operation; the patient died of occipital abscess. The other case which died was also not straightforward, being one of osteitis fibrosa.

He concluded by expressing the view that the operation was safe, and it had given him satisfaction.

L. Graham Brown said that he associated himself with those who had already spoken, particularly Mr. Negus, regarding the lines of treatment of the chronic condition, but he could not help wondering why surgeons did not draw a greater analogy between the frontal sinus and the antrum, and treat them in much the same way. He differed from Mr. Negus concerning the performance of an operation on the chronic sinus when the condition was well established—the history chiefly as well as the X-ray appearances would inform one on this point. He would not hesitate in such a case to make a further extension outwards of the incision at the inner canthus if this was necessary to get a good view of the cavity of the frontal sinus. Moreover he thought it was necessary to remove a membrane which was polypoid or which was actually very thickened. The latter was in fact a "pyogenic" membrane and if it was allowed to remain a bad result would ensue since it would go on forming pus. He thought the results of removing as much of the floor of the frontal sinus as necessary for the above purposes were satisfactory. Drainage into the nose by means of a large rubber tube should be carried out for quite ten days. The opening certainly cicatrized considerably, but so did the opening into the antrum, but there remained almost invariably sufficient aperture to drain the sinus.

T. B. Layton said that there were two causes of failure of operative surgery other than those indicated. One was the nature of the disease and the other was the fact of operation. Lister said that inflammation tended to get well by itself if the cause of the irritation were removed, and that was the reason why drainage was such a wonderful operation against the pyogenic reactions of the mucous membrane of the sinuses. But there was another reaction and that was the polypoid reaction. The cause of this was not as yet known. He was taught that it was the result of the suppurative reaction and that it was necessary to find which was the suppurative cell and to drain that. Then the rest of the mucous membrane would get well. This was the teaching of that great rhinologist F. J. Steward; but it was one of the few points on which his teaching was wrong. If they did not know the cause of the irritation in the polypoid antrum operative surgery would not cure it, because, after all, these operations came down to the question of drainage.

The other cause of failure was the fact of operation. If the diagnosis of frontal sinusitis were made on a headache, operation would make that headache worse, and if another operation were done it would be made worse still, while if there were a third operation that unfortunate person would probably have a headache for the rest of his life.

A suppurative sinusitis following the exanthemata was very rare indeed. The cases could be finally got well by correct treatment. Children who had had whooping-cough were examined to-day by X-rays and it was found that a very large number of them had got swollen mucous membranes in the maxillary sinus. Either that should not be labelled sinusitis or there should be an approach other than operative surgery.

Musgrave Woodman said that most acute cases resolved under conservative treatment and he never operated at all if it could be avoided. A direct opening into the frontal sinus for drainage in the acute stage would as a rule prevent a chronic sinusitis arising. Mr. Howarth was not quite right when he said that if the operation failed it was the surgeon's fault. He found skin-grafting of the frontal duct a difficult procedure and one liable to fail. Mr. Layton was probably mistaken when he talked about the absence of sinusitis following exanthemata. The fact was that most of these patients were ill and in a state of depressed vitality and had not sufficient power of reaction to form pus in a sinus.

The President said that he agreed with Mr. Negus as to the value, in some cases, of Kisch's operation. He had found that, owing to the limited removal of the floor there was less tendency, in this operation, to closure of the fronto-nasal opening. There were cases, however, in which complete removal of the lining membrane was essential. There were obvious advantages in an approach through the anterior wall, leaving the orbital contents intact. He would like to have heard the views of those with experience of Lothrop's operation.

Bedford Russell, in reply, said that he agreed with the President's remarks about the taking away of the supports; that was one difficulty in operations carried out by the external approach. He had devised an aseptic drainage operation through an external incision where one removed the bone but did not transgress the mucous membrane. He operated on some of these cases twenty-four years ago and saw one of them recently, in which a cannula would pass easily into the frontal, and where there had been no return of headache.

Colonel Canfield had mentioned the question of pain persisting in spite of operation on the sinuses. He himself had had one or two such cases. They seemed at the outset to need operation, but showed no improvement in the symptoms afterwards. Colonel Canfield had said that the pain was always due to pressure, but with that he could not agree. Pressure was not present and had not been present since the operation in three of the cases in his experience, but hyperæsthesia was present. He believed that a neuritis or perineuritis of the gasserian ganglion accounted for the pain persisting after operation in these people, and he still had hopes of the neuritis subsiding.

He agreed with Mr. Layton in that he recognized suppurative and polypoid types of sinus trouble. But he disagreed with him in his poor opinion of the results of operation on polypoid cases.

A cause of failure in chronic frontal operations was that one had omitted to deal with the other frontal sinus. He agreed that prolonged pressure in the frontal was often shown by absorption of either anterior or posterior wall, and it was necessary therefore in cases of an anterior perforation to keep in mind the possibility of a frontal lobe abscess.

Colonel Canfield said that it would now appear that as tantalum could be tolerated they did not need to be quite so conservative in the removal of bone, because the defects could be repaired at a later operation by means of tantalum.

Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[January 5, 1945]

DISCUSSION ON EXTRADURAL SPINAL BLOCK

Dr. C. J. Massey Dawkins : Extradural spinal block is a method of regional anæsthesia obtained by injecting an anæsthetic solution into the epidural space. It was first introduced in 1921 by Fidel Pages of Barcelona and was developed ten years later by Dogliotti of Milan. Since that date it has come into general use in South America and to a lesser extent in the U.S.A. and on the Continent, but there is no reference to it in the English literature whatsoever. The epidural space lies between the parietal and medullary layers of the dura mater. It is closed above by the fusion of these two layers at the foramen magnum and below by the posterior sacro-coccygeal ligament. It is pierced on either side by openings for all the spinal nerves. The interior of the space contains loose areolar tissue and numerous blood-vessels and it has an average diameter of about 4 mm. Experiments with lipiodol have shown that, if injected into the epidural space it diffuses along the nerve roots through the intervertebral foramina and comes to lie in the paravertebral tissue. This diffusion is quite rapid, experiments having shown that the pressure in the space produced by the rapid injection of 10 c.c. of saline, returns to normal in twenty seconds. It is in the paravertebral area that nerve block occurs when an anæsthetic solution is injected into the space, the injection being made, usually, in the lumbar or lower thoracic region. No absorption takes place through the dura mater, the anæsthetic effect beginning where the medullary layer fuses with the perineurium of the spinal nerve at the mid-point of the intervertebral foramen. In addition to the spinal nerve the grey and white rami communicantes of the sympathetic will also be affected, which fact constitutes one of the great advantages of the method. It is quite impossible for any anæsthetic fluid injected into the epidural space to reach the vital centres in the medulla.

It was discovered by Heldt and Moloney in 1928 that a negative pressure of -1 to -18 mm.Hg exists in the epidural space. This was confirmed by Bonniot (1934), who found, also, that the pressure could be increased tenfold by tipping the patient head down, which he ascribed to the effect of gravity on the cerebrospinal fluid causing a local increase of the negative pressure in the lumbar region. There are two theories to account for the existence of this negative pressure; first that a cone of depression is produced in the dura mater by the advancing needle point, thus creating an artificial space; secondly that there is no negative pressure when the spine is extended, on flexing the spine the vertebral canal is lengthened by separation of the vertebral arches and consequently the volume of the epidural space is increased, thus creating a partial vacuum, but only for a short time as there is a compensatory influx of venous blood. The recognition of this negative pressure is vital to the success of extradural spinal block and various methods have been evolved to demonstrate it. Sebrechts advised deliberate puncture of the dura mater and then withdrawal of the needle until the flow of cerebrospinal fluid ceased, but there are obvious defects in this method.

Dogliotti (1933) relies on the sudden loss of resistance to an injected fluid, he attaches a 2 c.c. syringe filled with saline to the spinal needle and maintaining pressure on the piston, observes the exact moment that the needle penetrates the ligamentum flavum, indicated by the sudden free movement of the piston. Gutierrez (1942) relies on the sign of the drop. He fills the needle with saline, leaving a drop hanging on the hilt, which drop is sucked into the needle by the negative pressure when the epidural space is reached. Odom (1936) has improved on this by fixing a capillary glass tube containing a bubble of air to the needle, movement of the bubble towards the spinal column being easily visible. If the needle is advanced too far and the theca is tapped, the cerebrospinal pressure will cause the bubble to move in the opposite direction. It is vital to be certain of the position of the needle tip, especially when making the puncture in the thoracic region where the puncture of the dura mater might lead to permanent damage to the spinal cord.

I first used this method of anaesthesia in a case of pulmonary tuberculosis, the operation being a second-stage thoracoplasty. The patient was extremely ill and a local anaesthetic was impossible as his first-stage wound had become septic. Any form of inhalation or intravenous anaesthesia would almost certainly have proved fatal, leaving epidural block as the only possible method. The operation was successful and although the patient died a few days later it was felt that the anaesthetic was not to blame. I have since extended the use of this form of anaesthesia to all thoracic operations and to many abdominal ones also. In an effort to obtain a greater margin of safety I have slightly modified Odom's technique. The indicator is permanently attached to the spinal needle as, if the joint is not airtight, a false movement of the air bubble may take place; also it is easier to handle all in one piece. A cannula has been made to fit outside the needle, allowing the needle to be removed when the epidural space is reached, leaving the blunt-ended cannula in position. This minimizes accidental penetration of the dura mater. Any type of local anaesthetic can be used, but I much prefer nupercaine because of its longer duration. I commenced using nupercaine in a strength of 0.1% but found that this was occasionally too weak, and I am now using 0.15% or 0.2%, the maximum safe dose at the latter concentration being 60 c.c. 20 drops of adrenaline (1:1,000) are added to limit spread and prevent toxic absorption. The solution is made up with half normal saline which gives a specific gravity of 1.0035, so that with the patient in the head-down position an accidental subarachnoid injection would diffuse away from the medulla.

The anaesthesia produced in extradural spinal block is almost entirely a sensory one, the motor nerves being little if at all affected. This fact is of the greatest importance as it enables operations to be performed on any part of the body, except that supplied by the cranial nerves, without danger of respiratory failure due to paralysis of the phrenic nerves. The reason for this selective action is probably to be found in the relative sizes of the motor, sensory and sympathetic nerve fibres. The motor nerve fibres have an average diameter of 2-20 μ , while the sensory and sympathetic fibres have an average diameter of $\frac{1}{2}$ -2 μ ; the anaesthetic solution penetrates the smaller fibres with much greater ease. Also, the dura mater over the posterior root ganglion is much thinner than elsewhere and it appears possible that some absorption may take place with consequent paralysis of the ganglionic cells, which are entirely sensory. It has been found with continuous caudal anaesthesia, where the epidural space is approached from the sacral hiatus, that some motor paralysis does come on after ninety minutes, but it is never complete.

Technique: The patient is given morphine grain $\frac{1}{4}$ - $\frac{1}{2}$, according to age, together with atropine grain 1/100th three-quarters of an hour beforehand. If a thoracoplasty is to be done, the patient is given a tablet of amethocaine to suck; this is to enable an airway to be used, as the glossopharyngeal and vagus nerves will not be affected by the block. The patient is then turned on to his affected side with moderate flexion of the trunk and a 10 degrees head-down slope. After the usual antiseptic precautions a skin wheal with nupercaine is raised over the selected intervertebral space and the spinal needle complete with cannula and indicator is passed through the supraspinous and interspinous ligaments. The spine is then acutely flexed and the needle advanced through the ligamentum flavum until the sudden cessation of resistance, coupled with the movement of the air bubble towards the spine, indicates that the epidural space has been reached. The rate of movement of the bubble varies from a complete and rapid disappearance into the shank of the needle, to a slight movement of 1 mm. Vicente Ruiz (1935) in a series of 415 cases found this sign to be present in 84%, which corresponds exactly to my own experience. If no movement

occurs, puncture should be repeated in another space. On one occasion I had to make four punctures before a successful result was obtained. If there is still no sign of negative pressure, reliance must be placed on the feel of penetration of the ligamentum flavum or the attempt should be abandoned. It is exceedingly unwise to go on if one is not absolutely sure. In a few cases the dura mater will be punctured, when another space should be chosen; this has occurred in 14% of my own cases, but it can be avoided by increased technical accuracy. The epidural space having been localized, the needle is withdrawn, leaving the cannula in situ. A 10 c.c. syringe containing nupercaine is then attached to the cannula and this amount is injected. After five minutes the patient is asked to move the toes of his foot on the affected side. If he is able to do this then it is certain that the dura mater has not been punctured. If the toes are paralysed then an ordinary unilateral spinal block has ensued and further injection should be abandoned. If this has not taken place, 50 c.c. of nupercaine (0.15 or 0.2%) are injected slowly, five minutes being spent over this and repeated aspirations being made to make certain that the cannula has not shifted. Some alarm may be experienced when changing syringes, as some of the solution always drips out of the cannula owing to back pressure, simulating a spinal tap, but the flow soon ceases. As injection proceeds it will be noticed that both pulse and respiration are quickened and the patient may complain of headache or dizziness. This latter is probably due to increased pressure on the cerebrospinal fluid, transmitted to within the skull, and soon passes off. With the patient still on his side, 0.5 gramme of evipan is given intravenously together with ephedrine $\frac{1}{4}$ grain, an additional $\frac{1}{2}$ grain being given intramuscularly to prolong its action. As the extradural block takes twenty-five minutes to become fully established, the waiting period can be spent in putting the patient on the operating table, turning him on his opposite side, fixing the towels and the blood-pressure apparatus in position, &c.; the evipan allays the natural fears of the patient during this process. It is quite unnecessary to use pentothal, as only a hypnotic effect is desired. Finally the patient is given nitrous oxide and oxygen by means of a face-piece, the oxygen percentage being kept high. This is done in order that a positive pressure can be provided for the surgeon if required, and so that the patient shall remain quietly asleep throughout the operation. It is most undesirable to have the patient awake and able to hear the sound of ribs being cut, &c. B.P. readings are taken every ten minutes but most cases showed a fall of only 10 to 20 mm.Hg, and in several cases the reading at the end of the operation was higher than at the commencement.

When the operation is finished great care must be taken with the bandaging, owing to the fact that the sympathetic vasomotor control over a large part of the body is paralysed. It is essential to place the patient in a slight head-down position before the shoulders are raised; failure to do so may result in a fall of B.P. to zero. Even with the patient tilted a fall of 20 mm.Hg is to be expected, but this returns to normal soon after the patient is returned to bed. As there is no post-operative headache, it is unnecessary to raise the foot of the bed, as after a spinal anaesthetic. Consciousness is regained within a few minutes and analgesia persists for six to eight hours, the general post-operative condition being very much better than with any other form of anaesthesia. My experience with extradural spinal block embraces all forms of chest surgery, but in some operations such as pneumonectomy and apicolysis, traction on the lung will cause coughing, as the sensory supply is from the vagus nerve which is not anaesthetized. This can be overcome by the surgeon injecting a little nupercaine into the hilum of the lung. If this is impossible owing to adhesions, the vagus can be blocked in the neck. I have used extradural block, also, for gastrectomy, appendectomy, herniotomy, radical mastectomy, Caesarean section and the relief of labour pains. For operations involving both sides of the body the patient is turned on his back immediately the injection is finished. 45 c.c. of nupercaine is sufficient for gastrectomy and 35 c.c. for appendectomy. The intervertebral space chosen is usually that between the 1st and 2nd lumbar vertebrae. It will be seen that with this technique the range of anaesthesia depends entirely on the position of the patient and the amount of solution injected; the flow of solution can be directed towards the head or the lower extremities at will. The ages of patients ranged from 9 to 65 years. Although I have used the method in over 75 cases, I do not feel this is a sufficient number for any statistical conclusions.

An alternative and a much more exact method is to make the injection at the level of the nerve supply of the area to be anaesthetized. This method has the grave disadvantage that puncture of the dura mater might lead to permanent damage of the underlying

spinal cord, but it does permit the use of far smaller quantities of solution and the resultant anaesthesia can be predicted with great accuracy. Abajian (1943), realizing that the levels of the cord for splanchnic and sensory anaesthesia are quite different, divides the injection into two parts. Thus, for appendicectomy, the sensory nerves

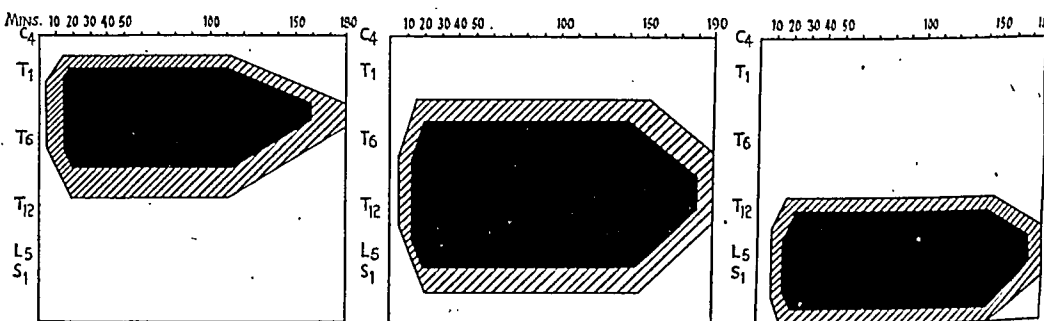


DIAGRAM OF ANAESTHESIA OBTAINED BY INJECTING:

FIG. 1.—25 c.c. of nupercaine between 4th and 5th thoracic vertebrae.

FIG. 2.—35 c.c. of nupercaine between 8th and 9th thoracic vertebrae.

FIG. 3.—30 c.c. of nupercaine between 4th and 5th lumbar vertebrae.

are blocked by 15 c.c. of solution injected between T12 and L1 while the splanchnic supply is blocked by a second injection of 10 c.c. between T7 and T8.

Passing to the effects of the completed anaesthesia we find that, first, it is not quite so complete as that obtained with a spinal; the sense of touch is occasionally not entirely abolished, though pain and temperature sensations are always absent. In a review of the literature I have found records of 6,453 cases, of which 4.2% required supplementary anaesthesia, but this figure varied between 83% and 1% according to the skill and experience of the anaesthetist. Gutierrez, who has had far more experience of the method than anyone else, improved his figures in this respect from 6% to 1% over a period of six years. Six deaths have so far been reported. The effect of the anaesthetic on the respiratory system is slight, recorded cases of paralysis amounting to 0.6%, probably due to inadvertent dural puncture. The pulse is usually unaffected but B.P. usually falls about 10 to 20 mm.; this is easily controlled by ephedrine. The fall is occasionally more profound; recorded cases amount to 1%, again due probably to dural puncture. To avert this fall in bad risk cases I always give the patient intravenous saline containing 1/250,000 of adrenaline, using the technique introduced by Frankis Evans (1944). Nausea and vomiting occur in about 10%, due probably to insufficient dosage. There is no effect on liver or kidney function; post-operative retention of urine is unknown and headache very rare. Drescik (1938) had the opportunity of examining the epidural space of a man killed accidentally after two previous extradural blocks and found no evidence of any change. The prolonged post-operative analgesia is of great value in warding off shock, in one of my cases it persisted for twelve hours.

Complications: (1) Failure to inject the solution into the epidural space: if the injection is given into the subarachnoid space death may result; if given into the inter-spinous ligaments severe backache will result. (2) The possibility of injury to the spinal cord when injecting in the thoracic region. Desplas (1934) records that one of his 83% failures had symptoms identical with those of hæmorrhachis for four days. (3) The possibility of injection into a blood-vessel, with resultant toxic effects, though this is unlikely if the mid-line is strictly adhered to. (4) Technical impossibility of injection, owing to calcified ligaments, to the fusion of the two layers of dura mater or to the presence of a spinal cord tumour.

The advantages of epidural anaesthesia over local anaesthesia are: (1) Complete segmentary anaesthesia, not merely anaesthesia of the body wall; (2) one injection instead of many—less solution is used—the injection takes one-fifth of the time and is much less of an ordeal for the patient; (3) there are no trophic disturbances of the skin; (4) post-operative wound pain is reduced; (5) there is no fluid to irritate the tissues and delay healing.

Compared with spinal anaesthesia there are: (1) Greater limitation of the anaesthetized area to the segments required; (2) no meningeal reactions or danger of meningitis; (3) much less fall of B.P. as the area of peripheral vasomotor paralysis is less; (4) the impossibility of spread to the medulla; (5) no post-operative headache or bladder troubles.

The disadvantages of the method are: (1) The rather difficult technique. This can be overcome by experience; before attempting injection, practice can be obtained in the recognition of the space when giving an ordinary spinal anaesthetic. If it is impossible to obtain an Odom's indicator, a varicose vein adaptor will serve nearly as well. (2) The time taken to produce anaesthesia, it being essential to wait for twenty-five minutes before allowing the surgeon to proceed. (3) The need for a conscious patient during the preliminary injection. This, again, can be overcome by experience; one is, eventually, able to recognize with certainty the position of the needle and the five-minute pause can be eliminated. If the patient must be unconscious, recourse can be had to the knee-jerk; it will be absent in five minutes if the dura has been punctured and spinal anaesthesia has resulted, whereas with an epidural injection it will not disappear for twenty minutes. (4) There is the failure of touch anaesthesia in 4%. To my mind this is not of much importance as all patients should have sufficient premedication, followed by nitrous oxide and oxygen, to keep them asleep during the operation, and this is sufficient to deaden the sense of touch if it be present.

To sum up, extradural spinal block is an eminently suitable anaesthetic for any operation which does not involve the cranial nerves. It has great advantages over paravertebral block and spinal anaesthesia and should, in the future, replace these methods altogether. If administered correctly it is the safest of all anaesthetics for a serious operation on a bad risk subject.

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Dr. A. H. Galley [Abridged] said that the nomenclature associated with the two techniques of *extradural spinal block* was in great confusion. The extradural space was also called the epidural and the peridural space. Until recently the variations had been used synonymously but the term "peridural" was fast becoming associated solely with the technique just described by Dr. Massey Dawkins. Extradural spinal block induced by injections through the sacral hiatus was popularly called "caudal analgesia", but this was, of course, equally a form of epi- or peri-dural spinal block; it was high time that some authoritative declaration were made to ensure a uniform, and less ambiguous, nomenclature when distinguishing between the two techniques.

Continuing, Dr. Galley said that he had become greatly interested in the differences between the manifestations of subarachnoid and extradural blocks. The nerve fibres concerned were grouped, by the physiologists, into three categories: "A", "B", and "C" [1]; perhaps their properties and functions would be more readily understood if they were tabled as follows:

CLASSIFICATION OF NERVE FIBRES. [1, 6]

Type of fibre	Stimulation threshold	Function	Effect of spinal block
"A" Large medullated 20-1 micron	Low	Skeletal motor fibres. Fibres from touch endings. Fibres from proprioceptor terminals (i.e. muscles, tendons, ligaments, joints, periosteum, &c.). Small fibres possibly subserving pain and thermal sensations	Muscle paralysis. Loss of touch sense. Loss of stretch-reflex and muscle tone, i.e. "relaxation"; also loss of joint sense, &c. Analgesia. Loss of thermal appreciation
"B" Small medullated < 3 micron	Medium	Most preganglionic sympathetic (involuntary) motor fibres. (White rami). (By definition this group is reserved for sympathetic motor fibres)	Vasodilatation. Loss of power of sweating in area affected. Loss of reflex action of pilo-motor muscles. Constriction of the bowel and relaxation of certain sphincters

CLASSIFICATION OF NERVE FIBRES. [1, 6] (*contd.*)

Type of fibre	Stimulation threshold	Function	Effect of spinal block
"C"	High	Some pre- and all post-ganglionic sympathetic motor fibres (grey rami). Afferents mediating sensations of pain and temperature—	Some sympathetic paralysis as above. Grey rami unaffected by subarachnoid block but may be affected in extradural block. Analgesia and loss of thermal appreciation
Small nonmedullated		40% of posterior root fibres are in this category [2]	
<1 micron			

Viscerosensory (enteroceptive) fibres belong to categories: "A" (small fibres) and "C"; they pass through the ganglia of the autonomic system (e.g. sympathetic paravertebral chain), uninterrupted, to their cells of origin in the posterior root ganglia [3, 5]. Thus *all* sensory impulses traverse the posterior roots (or cranial homologues).

Discrepancy between motor and sensory paralysis.—In subarachnoid, as well as extradural spinal block, there was always a discrepancy between sensory and motor paralysis; in subarachnoid block this was of the order of some two or three segments in favour of sensory paralysis; in extradural block, however, complete blocking of pain impulses usually occurred before there was any noticeable effect on the motor nerves.

Dr. Galley thought it highly suggestive that the facility with which neurones were paralysed corresponded fairly closely with the size of the fibres [7], which in turn was largely determined by the degree of medullation. At the one extreme were the pain fibres—all small and the majority nonmedullated [2]—these were the most readily blocked; at the other extreme were the motor fibres with thick medullated sheaths—the last fibres to be affected. Did the medullary sheath shield the axon cylinder from the effect of the analgesic solution? Was that protection proportional to the thickness of the sheath? This would give an anatomical explanation of the discrepancy.

Again, it would be noted that the stimulus threshold of the fibres varied in inverse proportion to the degree of medullation [4], pain fibres having a high threshold and motor fibres a low threshold—the other types of neurone intervening in order. What was more probable than the fact that analgesic drugs acted by raising the threshold? Pain fibres with an already high threshold could then be rendered insensitive in short time by elevating the threshold beyond the reach of any stimulus; motor fibres, when subjected to identical analgesic concentrations—having a low threshold—would require a longer time to produce a similar effect. This would provide a physiological explanation; it was even possible that the anatomical and physiological factors acted in concert.

Although the foregoing were reasonable explanations for these discrepancies, it did not explain the enormous discrepancy encountered in extradural blocks. If it were due to a difference in the thickness of the dural sheaths which continued along the anterior and posterior spinal nerve roots one would expect that sympathetic motor paralysis would lag behind with motor paralysis—this did not happen. An alternative explanation might be that fluid percolated along the perineural spaces of the common spinal nerves as far as the grey rami, which, as their name suggested, were nonmedullated. The subarachnoid space contained cerebrospinal fluid which acted as a vehicle and enabled smaller quantities of analgesic solutions to be employed; *but* the C.S.F. was also absorbed (among other places) along the perineural lymphatics of the spinal nerve roots—it probably took the analgesic along with it and brought it into more intimate contact with the nerve fibres. In extradural block, it might be that the analgesic solution was not brought into such intimate relationship and that the motor fibres—already protected by their superior medullation—were even more tardy in becoming blocked. All this was supported by the fact that fractional "caudal analgesia", if continued for long enough (e.g. during childbirth), produced an increasing motor paralysis which finally approached that seen in subarachnoid block. Also in support of the theory that the C.S.F. influenced the effect of analgesic solutions was the work of CoTui and Standard [8], who found that while an injection of procaine into the cisterna magna of a dog produced both respiratory and cardiovascular collapse, if the cisterna were opened, drained, and a pledget of cotton-wool soaked in a corresponding solution of procaine in C.S.F. were wrapped around the closed portion of the medulla and upper portion of the spinal cord, neither respiratory paralysis nor change in blood-pressure followed. They thought that the C.S.F. in the cisterna magna acted as a medium to carry the procaine into the 4th ventricle into more intimate relationship with the nervous tissue concerned.

Practical points.—The greater discrepancy between motor and sensory block in extradural analgesia made it the safer method of spinal block for Cæsarean section, as the intercostal muscles were less likely to be paralysed and thus further embarrass the respiratory mechanism already labouring under the disadvantage of having the diaphragm "splinted" by the uterine enlargement.

Once pierced, the dura remained patent [9, 10], and any solution injected would most probably produce subarachnoid block—a disastrous proceeding if the large volumes associated with extradural analgesia were injected.

Even when aspiration tests proved negative, a preliminary precautionary dose should always be employed—if subarachnoid block did not supervene, only then should the main dose be given.

In extradural block the likelihood of piercing vessels was relatively high: blood was alkaline and capable of precipitating the inactive base from the hydrochloride analgesic solutions in common usage. Furthermore, a hæmatoma in the sacral canal might limit the rise of the solution into the higher portions of the extradural space; this occasionally occurred as a delayed action, for the main dose temporarily limited the bleeding by mechanical pressure—after a while bleeding recurred, a hæmatoma supervened and topping-up doses failed to produce further analgesia above the sacral region.

Either form of extradural block was difficult of technique and tedious to perform—in addition, the incidence of failure exceeded that of subarachnoid block; these were, of course, only relative contra-indications to its use but would naturally influence anæsthetists when making a choice of anæsthetic.

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Major R. A. Gordon, R.C.A.M.C.: We first used extradural spinal block in December 1941 in our plastic service. The object was to produce adequate analgesia of considerable length with maintenance of muscle tone for the operation of crossed-legged skin flap. Our first efforts were not considered satisfactory but good results have been consistently obtained in a considerable number of patients where the block has been done in a sitting position, the injection being made in the second or third lumbar interspace. It must be remembered when this type of analgesia is employed for operations on the lower extremity that the fibrous attachments of dura to the bony canal may be so dense as to prevent spread of the anæsthetic solution to the sacral roots. In some cases it has been necessary in addition to perform extradural caudal block.

The following points of technique have, I think, contributed to success in use of this type of anæsthesia:

(1) The use of a large bore (16 S.W.G.) needle with a sharp short bevel. Such a needle will not pass through the dura as readily as one of smaller calibre. If a spinal tap is inadvertently made there will be immediate free return of fluid.

(2) The demonstration of the epidural space when a large needle is used is most simply done by relying on the sudden absence of resistance to injection when the needle enters the space. This method is equally reliable at all levels and has the advantage that if considerable force is applied to the plunger of the syringe as the needle point passes through the ligaments, the dura will most certainly be forced away from the needle point when the injection is made.

(3) Lateral approach has been used in our later cases, the needle passing through the ligaments very near the mid-line, and at such an angle that with the bevel of the needle directed towards the spinal canal it will be as near as possible flush with the wall of the canal on emergence. It is felt that this further reduces the possibility of inadvertent puncture of the dura.

(4) The injection must be made slowly so that the fluid will diffuse over the greatest possible length of epidural space. As Dogliotti has pointed out, any considerable pressure developed in the epidural space by rapid injection will result in dispersion of the solution along the nerve roots in the immediate vicinity and will definitely reduce the number of segments anesthetized by any given volume of solution.

[March 2, 1945]

Experiments in Artificial Respiration and in Asphyxia [Abstract]

By R. R. MACINTOSH, D.M., D.A.

THIS short paper discusses three problems which required for their elucidation a human subject anesthetized under hazardous conditions. The problems were propounded by, and the experiments carried out on, Squadron Leader E. A. P.

WHAT IS THE MOST EFFECTIVE METHOD OF ARTIFICIAL RESPIRATION?

The answer cannot be obtained from experiments carried out on the conscious subject.

E. A. P. volunteered to be anesthetized deeply and rendered apnoëic after forced ventilation. A condition of passivity resulted, resembling the moribund patient. The various methods of artificial respiration were now carried out, inspirations and expirations being recorded on a moving drum.

Eve's method.—The strikingly good exchange of 560 c.c. takes place when the patient is rocked through 90 degrees in the prone position. A decrease in the angle of rocking diminishes the exchange, as also does placing the patient in the supine position. The exchanges effected on the same subject by the Schafer and Silvester methods were found to be 340 and 400 c.c. respectively. Many other manual methods and modifications were tried but none approached the figures of Eve's which were exceeded only by the positive pressure methods of inflation. The Oxford Inflator, a simple mechanical device for inflating the lungs with oxygen at a pressure of 40 mm.Hg gave an exchange of 970 c.c. and mouth-to-mouth inflation a similar reading. This series of experiments was repeated on another volunteer, Dr. John Roberts, and the findings correspond closely. The fact that these figures are high can be explained by the various methods of artificial respiration being performed in ideal circumstances. A wide-bore endotracheal cuff-tube ensured a clear airway, the subjects were healthy young males, and the operator highly skilled.

Eve claims that the venous return to the heart and therefore the output from the heart is improved more by his method than by others. The figures I have given record only pulmonary ventilation. I have held for many years that the choice of anæsthetic agent matters little compared with the skill of the man who administers it, so do I believe that in artificial respiration the operator matters more than the method. If the subject is dead no method will avail and, broadly speaking, if a spark of life still exists, any method—properly carried out—will probably suffice.

UNCONSCIOUS FLOATING POSITION

There are many different types of life-jackets available in the various Services. These should keep the individual afloat with his head out of water even though he loses

consciousness. Nevertheless, from time to time victims are found floating with their faces submerged and, of course, drowned. The true floating position can be ascertained only on the unconscious subject since the conscious individual can assume or retain almost any floating position by very slight alterations in muscle tone. [A film was then shown in which E. A. P., anæsthetized through a cuff-endotracheal tube, and wearing different life-jackets, was placed in good and in unfavourable positions in the swimming bath. The self-righting properties of the various jackets were assessed. Without a jacket the subject sank to the bottom of the bath.]

AN EXPERIMENT IN ASPHYXIA

What is the maximum height from which a man can bale out of an aircraft and, breathing air, descend by parachute without dying of asphyxia? The *percentage* of oxygen in the atmosphere remains unchanged at 20 whatever the altitude. At ground level the oxygen exerts a *pressure* of 160 mm.Hg forcing its way vigorously as it were into the blood-stream via the lungs. With increase in height the partial pressure of oxygen in the atmosphere gradually falls until at the enormous height of 40,000 ft.—over seven miles—a height at which flying is carried out nowadays, it is only 30 mm.Hg. The anoxia which results from breathing air at high altitudes can be reproduced experimentally at ground level by inhaling an artificial mixture of oxygen in nitrogen. For example, breathing air at 20,000 ft. at which the barometric pressure is 350 mm.Hg, results in a partial pressure of oxygen in the alveoli of 41 mm.Hg. This effect can be reproduced at ground level by breathing a mixture of 10% oxygen in nitrogen. Breathing air at 35,000 ft. gives an alveolar oxygen tension of 15 mm.Hg, and this can be reproduced by breathing 4% oxygen at sea-level. Similarly conditions at 40,000 ft. are reproduced by 2% oxygen at sea-level.

In the early stages parachute descent is at about the rate of 2,000 ft. per minute, and as descent continues, there is a gradual increase in atmospheric pressure and in alveolar oxygen tension. The improved oxygenation resulting from the descent can be simulated at ground level by an increment of 1% oxygen to the experimental mixture each minute.

To simulate a descent by parachute from 40,000 ft. therefore the victim is asphyxiated with a mixture of 2% oxygen in nitrogen for one minute; at the end of the minute the oxygen is increased to 3%; at the end of the second minute to 4%. By the end of the third minute the condition of the patient is grave. He has passed being blue—he is grey, sweating, twitching horribly and gasping, yet the oxygen is increased only to 5%. E. A. P. and the other volunteers for this experiment were all medical men, familiar with Courville's book on "Upward Effects of Nitrous Oxide" and of the grave potentialities of prolonged asphyxia. These experiments were carried out with the volunteer suspended from the roof in parachute harness. The weight of the body pulling downwards forced the suspension straps into the chest considerably impeding free respiration.

In the actual experiments heights known to be safe were started with. At 35,000 ft. for example, consciousness was lost, but never at any time was anxiety caused. 40,000 ft. was regarded as the absolute limit from which a jump can be made in these conditions with a reasonable prospect of survival.

The following is a brief report on two subjects investigated conjointly with Professor R. R. Macintosh: (I) On Intrasternal Anæsthesia and (II) on Bilateral Vagus Block.

I.—Intrasternal Anæsthesia [Abridged].—WILLIAM W. MUSHIN, M.B., B.S., D.A.

The sternal medulla contains red bone-marrow which communicates freely with the vascular system. Since 1941 it has been used for giving a variety of fluids [1]. We confirm the value of the sternal route for giving anæsthetics. Its reliability justifies its use in preference to the intravenous route in ophthalmic and other operations where dislodgment of the needle from the vein would interrupt the smooth course of the operation.

The sternal medulla is easy to enter and once the needle is in place does not slip out. The needle penetrates the outer plate of the sternum in the mid-line, opposite the 2nd intercostal space. Aspiration of blood-like medullary contents confirms that the point of the needle is correctly situated. A drip-feed of anæsthetic solution is

attached and the procedure from now on is identical with intravenous anaesthesia. Any anaesthetic which can be given intravenously can be given by the sternal route. To ensure good control we favour weak solutions (e.g. 0.5% pentothal) which can conveniently be given through the apparatus described by Macintosh and Pask [2]. We also favour a 1% solution of avertin, which we have used intravenously for many years; its administration by the sternal route is attended by equally happy results.

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II.—Bilateral Vagus Block [Abridged].—WILLIAM W. MUSHIN, M.B., B.S., D.A.

A bilateral block of the vagus [1] at its exit from the skull interrupts fibres to and from the larynx, trachea and bronchial tree as well as the other organs supplied by these nerves. The patient cannot talk, and his cough reflex is lost. The effect on the parasympathetic fibres is the same as that produced by a full dose of atropine. The vagus here lies anteromedial to the internal jugular vein in close proximity to the cervical sympathetic and the ninth, eleventh and twelfth cranial nerves. Some involvement of these invariably accompanies vagal paralysis. Horner's syndrome develops quickly. The voice becomes nasal, then hoarse, finally disappearing to a whisper. Swallowing becomes impossible. Should the hypoglossal nerve be paralysed, the patient must be supervised as if he were unconscious. Otherwise the paralysed tongue may fall back, giving rise to the paradoxical situation of grave respiratory obstruction in a conscious patient. Since the vagal fibres are interrupted, laryngoscopy can be performed and the cords seen to be motionless. A tube can be passed between them without eliciting reflex response. We have used this block 50 times for major operations on the larynx and oesophagus, as well as for endoscopy. The absence of coughing which follows suggests that vagal block may have a place in anaesthesia for thoracic surgery. The disadvantage of this procedure is the absence of landmarks which ensure that the solution will be deposited with certainty in contact with the vagus.

REFERENCE

- 1 BERTOLA, V. J. (1940) *Prensa méd. Argent.*, 27, 1060.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[February 23, 1945]

The International Sanitary Convention of 1944

By P. G. STOCK, C.B., C.B.E., F.R.C.P.

INTERNATIONAL Sanitary Conventions are of interest to epidemiologists as they represent the practical application of accumulated medical knowledge and are designed to prevent or control the spread of epidemics from one country to another with the minimum of inconvenience to international traffic.

To understand the new Conventions, and the reasons which led to their being drawn up during the turmoil of a great war it is desirable briefly to review the history of International Sanitary Conventions which govern the maximum measures that may be imposed at sea or air ports to prevent the importation of the more dangerous infectious diseases by means of maritime commerce or air travel.

Such measures are even now commonly spoken of as "Quarantine" but the word quarantine has long lost its original meaning and thanks to the progress of medical knowledge the old days when vessels might be burnt or mariners hanged in an attempt to prevent disease being introduced have passed for ever.

Nevertheless it is of interest to recall that as late as 1833 under the Quarantine Act of Western Australia [1], which expressed the official attitude of the period, if a vessel were liable to quarantine and had not entered at one of the ports prescribed, then the Master might be obliged "either by firing of guns upon such vessel or by any other kind of necessary force whatsoever" to proceed to a port appointed for the purpose. And, that even in 1865 when the sailing barque *Hecla* arrived at Swansea with cases of yellow fever on board and the disease afterwards spread to the town, so much alarm was created that the vessel was sent to sea under threats of being burnt if she lay in the dock another night [2].

The introduction of plague (or the black death) from the Crimea to Genoa in the fourteenth century led to attempts at maritime quarantine and the Quarantine Code drawn up in Venice in 1348 served for hundreds of years as a model to other countries. In England in 1664 Quarantine Regulations were adopted which aimed particularly at control of infection coming from the Levant and took into account both the state of health of the port of departure and the state of health of the ship before departure *but not during the voyage*. They included provisions that no vessel should leave any port in Turkey or Egypt without a Bill of Health and no Bill of Health was to be given until the expiration of forty days from even a single case of plague in the port of departure. Bills of Health can therefore perhaps be considered as the early forerunner of the modern system of international epidemiological information. They have long outlived any useful purpose they originally served and have been supplanted by the cable and "wireless" but it is only in the Convention of 1944 that definite provisions have been made for their abolition. Up to 1710 when the first Quarantine Act of Parliament was passed in England, all restrictions in England were in the shape of regulations issued by the King in Council. The history of quarantine procedures is not the subject of this paper but one provision of the Act of 1710 may be quoted as indicating the grounds on which trouble might have arisen if this practice had been applied to foreign shipping and the need for some international code. In the second section of the Act it is enacted that "After the 25th December, 1710, if any Master, etc. shall go on Shoar, etc. or permit any person so to do, without licence, the ship etc. shall be forfeited to the Queen".

Countries generally were concerned only in attempts to protect themselves against "pestilence" brought to their shores and it was only under the urge of the great cholera outbreak in Europe in 1848-50 that the first steps were taken to create some international co-operation in maritime quarantine. (In England and Wales alone in 1848-49 about 72,000 persons fell victim to the disease [3].) Moved by the varying regulations governing maritime quarantine, the French Government in 1851 convened the first international conference to discuss the adoption of a uniform code, and a

attached and the procedure from now on is identical with intravenous anaesthesia. Any anaesthetic which can be given intravenously can be given by the sternal route. To ensure good control we favour weak solutions (e.g. 0.5% pentothal) which can conveniently be given through the apparatus described by Macintosh and Pask [2]. We also favour a 1% solution of avertin, which we have used intravenously for many years; its administration by the sternal route is attended by equally happy results.

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Sanitary, Maritime and Quarantine Board of Egypt (Articles 163-167 now amended) and Part V contains the final provisions regarding ratification, &c.

Time does not permit of any detailed analysis of this Convention but it should be emphasized that the Convention provides for the immediate notification by every Government to other Governments and to the Office international d'Hygiène publique of cases of plague (including rodent plague), cholera, yellow fever, epidemic typhus and smallpox—often spoken of as the five "Convention" diseases. When the 1926 Conference was held delegates still had in mind the disastrous Pandemic of Influenza in 1918-19 but a proposal to include influenza among the diseases dealt with by the Convention was not accepted. The Convention prescribes the measures which must be taken in ports to prevent the exportation of infection by vessels and also those which may be applied to ships on arrival. These latter measures are laid down as maxima beyond the limits of which Port Health Authorities may not go, the spirit of the Convention being to avoid unnecessary interference with ships, passengers and cargoes by rigid quarantine methods and to rely on the quick detection of the occurrences of infectious disease.

With the development of international air traffic¹ it soon became apparent that some analogous code must be drawn up to apply to aerial navigation and the Committee of the Paris Office, in consultation with the International Commission on Air Navigation drafted the text of a Convention which after consideration by Governments and redrafting was circulated as a final text in 1932, opened for signature at the Hague in 1933 and following ratification by ten countries formally came into force in 1933 as the International Sanitary Convention for Aerial Navigation (1933). This Convention has not been so widely accepted as the International Sanitary Convention of 1926 and in the Western hemisphere has only been ratified or adhered to by Brazil, Bolivia, Chile and the United States.

The Convention deals with the five "Convention" diseases (plague, cholera, yellow fever, typhus and smallpox) and the measures prescribed are again to be regarded as a maximum. Definitions are given, for the purposes of the Convention, of authorized, sanitary and anti-aircraft aerodromes, &c., and a detailed code is provided against the spread of yellow fever by air traffic. Bills of Health "which in modern times have proved such an irksome and profitless formality in the case of shipping"[4] are not required.

There are various other International Conventions or Agreements dealing with health matters but they are outside the scope of this paper and we can now proceed to the Conventions of 1944 and the reasons for their preparation.

On November 9, 1943 (after much preliminary work both in this country and the U.S.A.), the representatives of the 44 United and Associated Nations signed at the White House, Washington, an agreement establishing the United Nations Relief and Rehabilitation Administration—commonly spoken of as UNRRA. The next day the representatives of these nations met at Atlantic City, in the First Session of the Council established by the agreement, to provide for the organization of the Administration and to lay down the broad policies to guide its activities. Only two of the aims and activities of UNRRA concern us to-day, viz.: The giving of aid in the prevention of pestilence . . . and the return of prisoners and exiles to their homes. The exact number of exiles or "displaced persons" is not known but it was estimated that there were in Europe alone, in the summer of 1944, at least 10,000,000 persons outside their own national territory.

It was also estimated that the chief diseases to be guarded against were epidemic (louse-borne) typhus fever and malaria, but outbreaks of relapsing fever, smallpox, diphtheria, scarlet fever, cerebrospinal fever, influenza, dysentery, the typhoid fevers, Asiatic cholera and the infectious diseases of childhood may occur. A high prevalence of certain other communicable and deficiency diseases, such as pulmonary tuberculosis, rickets and scurvy will also be encountered.

To advise the Administration of UNRRA on the health aspects of these problems a health Committee was set up. The special health problems of displaced persons and the fear of epidemics in countries, liberated from German and Japanese barbarism, pointed to the necessity for making adequate plans to deal with the conditions envisaged and this led to the examination of the International Sanitary Conventions of 1926 and 1933 with a view to appraising whether additional or amending powers were required. As Paris was then in enemy hands and no help could be obtained from the Office international d'Hygiène publique, two expert Commissions were appointed, viz. one on the health problems of "Displaced Persons" and the other on Quarantine. The recommendations of the Commission on the health problems of displaced persons were adopted by the European Committee of UNRRA and they form the basis of a draft

¹ The Atlantic was first flown in June 1919 by Alcock and Brown, and the first flight from England to Australia was made in November 1919 by Ross Smith and Keith Smith, who traversed over 11,000 miles.

Convention, based largely on the then existing French practice, was drawn up but this was hardly a success and was only ratified by three countries.¹

Between 1851 and 1903 nine other conferences were convened by various governments and though progress was made—for instance at Washington in 1881, when official recognition was first given to a limited exchange of epidemiological information and at Paris in 1894 when mutual arrangements were settled for the Mecca Pilgrimage—it was not until 1903 that a conference in Paris prepared the first International Sanitary Convention which dealt both with cholera and with plague and recognized the part played by rats in the spread of the latter disease. This Conference also adopted the proposals, first made at Vienna in 1874, to establish an international health office and under the Agreement drawn up in Rome in 1907 the Office international d'Hygiène publique was established in 1909 with permanent headquarters in Paris.

The Pan-American Sanitary Bureau, with headquarters in Washington, had already been established in 1902, and carries out for the Republics of North and South America work similar to that which the Paris Office did for the world generally. It also functions as a regional bureau of the Office international d'Hygiène publique under the International Sanitary Convention of 1926. Two other quasi-international bodies also existed when the Paris office was set up, viz. the Constantinople Superior Board of Health which dated from 1838 and the Quarantine Board of Egypt whose beginnings go back to 1831 when Mahommed Ali called on the European Consular body in Alexandria to organize and apply measures against plague and other infectious diseases.

The Constantinople Board of Health maintained a sanitary service (1) at the chief ports of the Black Sea, in the Dardanelles and on the coast of Asia Minor (2) in the Red Sea and for the Mecca Pilgrimage and (3) on the Turko-Persian frontier and for the Shiah pilgrimage. Its functions came to an end at the outbreak of war in 1914 and it was formally wound up in 1923 under the Treaty of Lausanne.

The Quarantine Board of Egypt, which in a large measure was regulated by successive International Sanitary Conventions, had its headquarters in Alexandria. Its main functions were the protection of Egypt from invasion by infectious diseases on its frontiers, particularly its seaports, and the protection of the countries in the Mediterranean and beyond by means of the control it exercised over the transit of vessels arriving from the South and passing through the Suez Canal. In addition it had various special health responsibilities in regard to the Mecca pilgrimage and pilgrim ships. It was abolished and its powers were taken over by the Egyptian sanitary authorities early in 1939 under the International Sanitary Convention of 1938 which modified the articles of the International Sanitary Convention of 1926² pertaining to the Sanitary, Maritime and Quarantine Board of Egypt as it was then named.

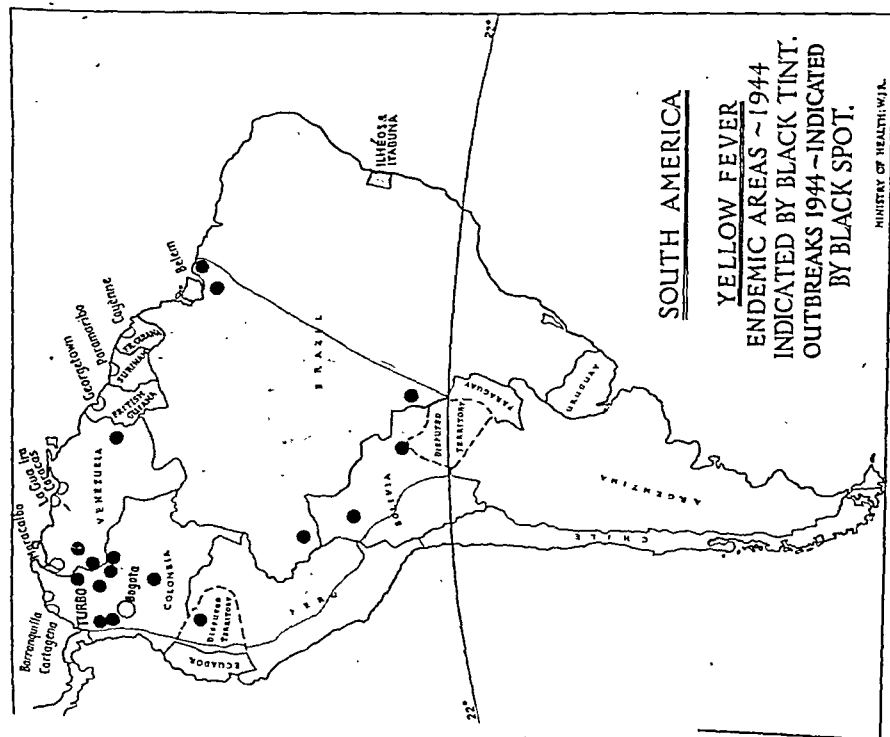
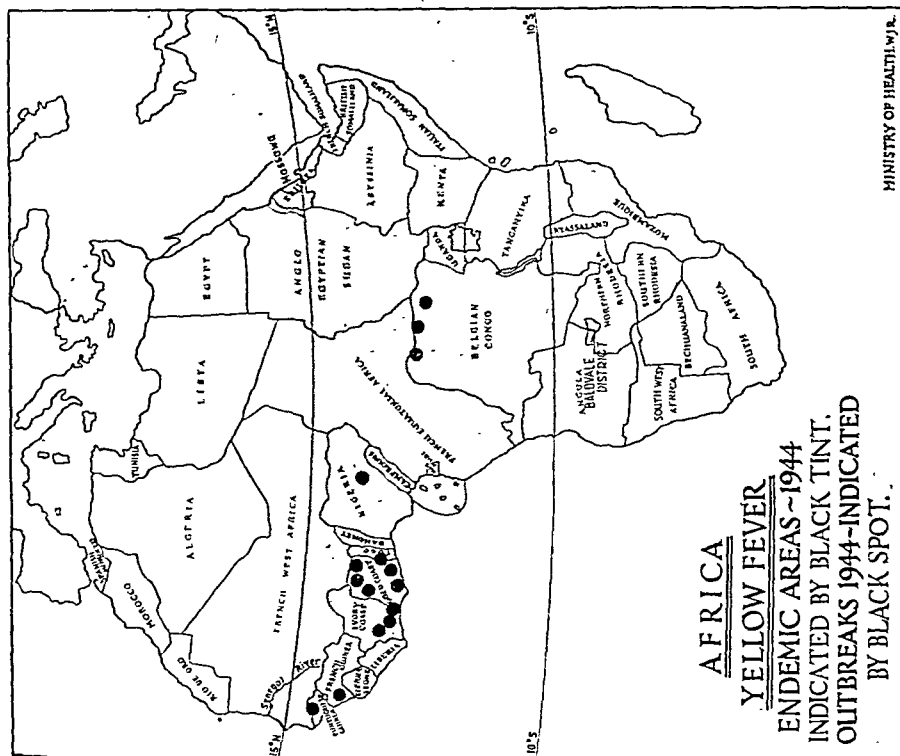
To return to the history of the International Sanitary Conventions the growth of epidemiological knowledge gradually rendered out of date the provisions drawn up in 1903 and in 1912 following a conference in Paris a new Convention was prepared.

When the Office international d'Hygiène publique resumed its international activities after the Great War of 1914-18 several sessions of the Permanent Committee were devoted to preparing a New Convention and after a formal conference in Paris, which lasted several weeks, the International Sanitary Convention of 1926 was signed by the representatives of 66 countries and subsequently ratified by 44.

As this Convention is still in force, though modified by the amending International Sanitary Convention of 1944, a very short summary of its principal provisions must be given. After some preliminary definitions the Convention is divided into five parts. Part I deals with provisions to be observed by the Governments of countries which are contracting parties to the Convention, on the appearance in their territory of plague, cholera, yellow fever, epidemic typhus and smallpox and the measures to be taken against the spread of these diseases (Articles 1-66). Part II deals with special provisions for the Suez Canal and neighbouring countries (Articles 67-90). Part III gives the special provisions regarding pilgrimages (Articles 91-162). Part IV deals with the

¹ Following the failure of the 1851 Conference the French Government called another conference in 1859 in Paris which drew up a Convention on much broader lines. Political events in Europe doomed this Convention also to failure, but in 1866 the French Government again convened a conference this time in Constantinople which met with greater success, particular attention being paid to cholera owing to the fear of its spread by the Mecca pilgrims. Eight years later, in 1874, the Austrian Government at the instance of Russia, convened a conference in Vienna which adopted principles of quarantine, much in line with modern practice and suggested the establishment of a permanent international sanitary commission. The next conference was convened by the United States at Washington in 1881 when official recognition was first given to the international notification of the more dangerous infectious diseases. Other conferences followed: at Rome in 1885 and at Venice in 1892 when, as a result of the generally felt need to control the introduction of cholera from the East into the Mediterranean basin, via the Suez Canal, which had been opened in 1869, a formal sanitary convention between countries first appeared. These agreements were extended by a conference in 1894 at Dresden, while in 1894, another international conference in Paris settled mutual arrangements for the sanitary regulation of the Pilgrimage to Mecca and questions of quarantine in the Persian Gulf.

The revival of plague in Bombay in 1896 and its rapid extension to various parts of the world led to a conference in Venice in 1897 and a further conference in Paris in 1903.



of the British Interdepartmental Committee on Yellow Fever Control and of the experts in the United States, but as the subject is highly technical and the Memorandum is shortly to be published by UNRRA, further reference is outside the scope of this paper. As complying with the standard laid down, the Commission recommended approval of the yellow fever vaccines prepared by the National Institute of Health, the United States Public Health Service, and by the International Division of the Rockefeller Foundation. They also recommended that vaccine similarly prepared (except that the drying is not carried out to the same degree) in the yellow fever laboratories in Rio de Janeiro, in Bogota, and in the Wellcome Institute, London, should, for the time being, be approved for quarantine purposes provided the inoculations are performed by officials of a national yellow fever service or by other medical officers properly authorized by their governments to do so.

In addition to the responsibility placed on UNRRA to lay down standards with which yellow fever vaccine must conform, UNRRA is required, in consultation with the Governments concerned, and, as regards the Western Hemisphere, with the Pan-American Sanitary Bureau, to designate from time to time Institutes which are approved for testing the activity of yellow fever vaccines. In order that UNRRA may comply with this obligation, the Commission recommended that the necessary steps should be taken with a view to the following laboratories being designated as Approved Institutes namely:

Bogota—Yellow Fever Laboratory, National Yellow Fever Service.

Entebbe (Uganda)—Yellow Fever Institute.

Hamilton (Montana)—Rocky Mountain Laboratory, National Institute of Health.

London—Wellcome Research Institute.

New York—Laboratories of the International Health Division, Rockefeller Foundation.

Paris—The Pasteur Institute.

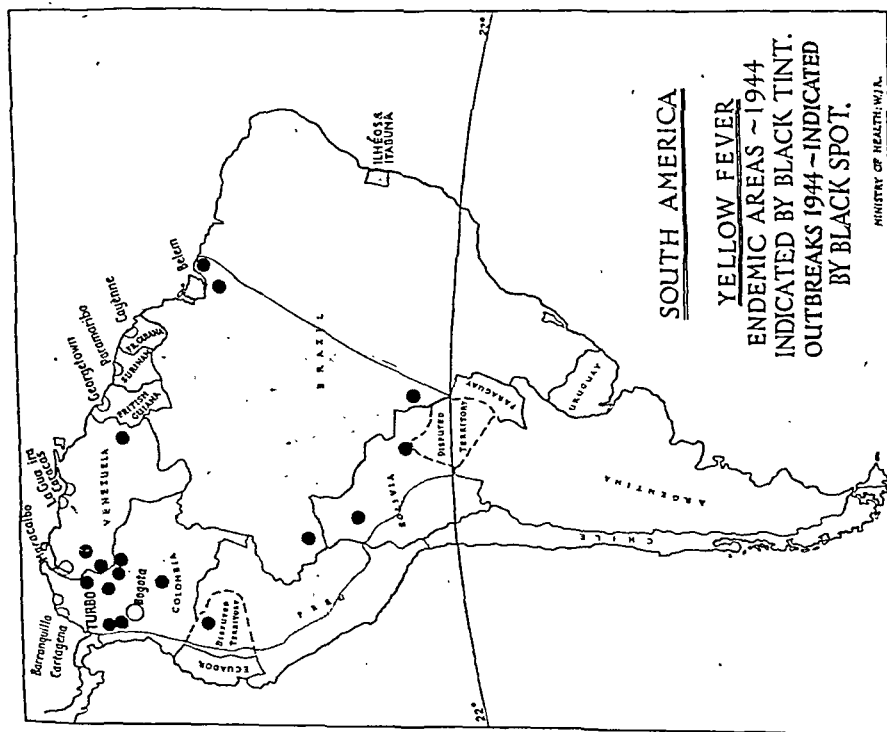
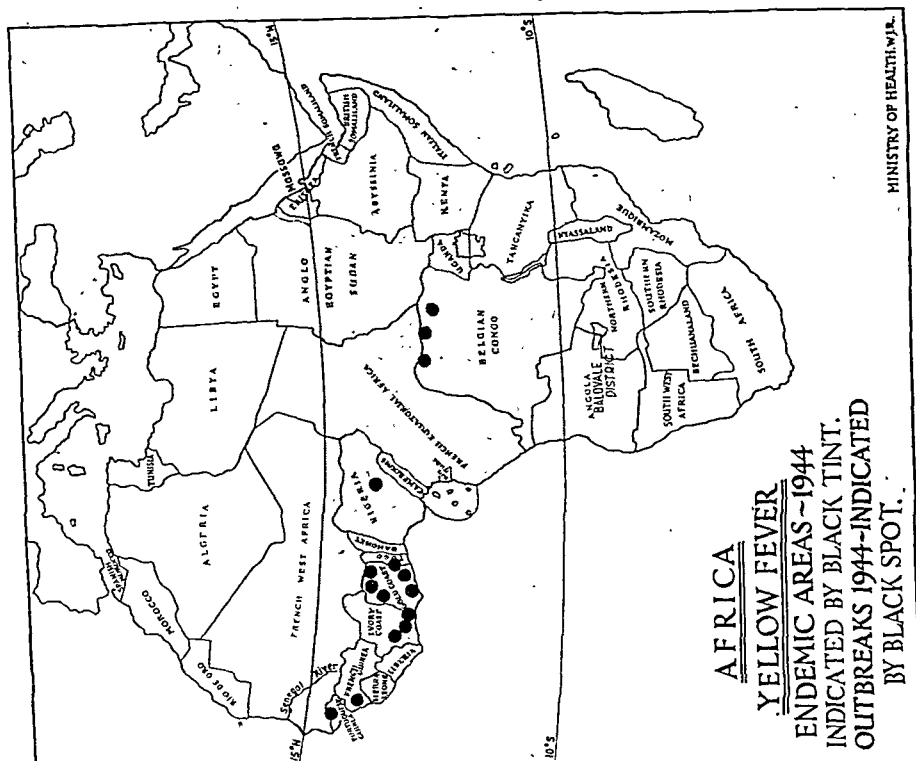
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In the delineation of endemic yellow fever areas in Africa the Quarantine Commission had the advantage of the views of the London Interdepartmental Committee on Yellow Fever Control [5], whose recommendations were adopted, and equal agreement was reached with the Pan-American Sanitary Bureau in regard to the Western Hemisphere.

For purposes of quarantine control the endemic area in Africa is defined as bounded by a line running from the mouth of the Senegal River along that river eastward to the 15° N. parallel of latitude, thence eastward along that parallel to the eastern border of the Anglo-Egyptian Sudan, thence northward along that north-western boundary of Eritrea to the Red Sea Coast, thence southward along the eastern coast of Africa to the southern boundary of the Protectorate of Kenya, thence westward along that boundary and southern boundary of Kenya Colony to its junction with the southern border of the Uganda Protectorate, and thence along this and the eastern border of the Belgian Congo to the 10° S. parallel of latitude, thence westward along that parallel to the west coast of Africa; thence northward along the west coast of Africa to the mouth of the River Senegal; including the islands in the Gulf of Guinea. The Committee also recommend that the *Balovale District* of Northern Rhodesia should be regarded as an endemic area, but for the time being the Port of Massawa in Eritrea should be excluded.

In the Western Hemisphere, for the purpose of quarantine control, the areas in the South American Continent which, for the time being, should be considered as endemic yellow fever areas are bounded by a line running from Turbo, in the Northern part of Colombia directly south to the northern boundary of Ecuador and then along the Eastern slopes of the Andes, below an elevation of 6,000 feet, to the northern boundary of Argentina, thence east along the 22nd parallel of latitude to the western border of Brazil, thence in a north-eastward direction to the junction of the States of Maranhão and Pará on the Atlantic Coast of Brazil, thence along the Atlantic and Caribbean coasts of South America to Turbo, excluding, however, the ports of Belem, in Brazil, Cayenne in French Guiana, Paramaribo in Surinam, Georgetown in British Guiana, La Guaira and Maracaibo in Venezuela, and Barranquilla and Cartagena in Guiana, and the cities of Caracas in Venezuela and Bogota in Colombia. In addition, the Isthmus of Panama from the Canal Zone to the border of Panama and Colombia and the Ilhéos and Itabuna districts in the State of Bahia in Brazil are for the time being regarded as endemic yellow fever areas.

The Commission further suggested that the authorities of any territories at present included within the boundaries of an endemic area who may wish to have any part excluded, should furnish UNRRA with the following information in regard to the part of the territories involved: (a) Evidence in regard to the risk of yellow fever infection; (b) particulars of measures taken to control *Aedes aegypti* so as to maintain



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Section of Psychiatry

President—A. F. TREDGOLD, M.D.

[March 13, 1945]

Subjective Psychological Responses of Patients Undergoing Physical Treatment in Mental Disorders. An Attempt at Clinical Evaluation [Abstract]

By JAN FRANK, M.D. Prague

DESPITE the established clinical value of physical treatments in the major psychoses, it remains important to observe the conscious, and as far as possible, subconscious individual reactions. Although no rationale which would be scientifically explainable has been found, the same artificially induced fit is applied, like a steamroller in its uninspired uniformity, in cases ranging from involuntional melancholia through manic-depressives and schizophrenias to symptom-neuroses. The inference is that either there is some common denominator in these varied conditions, or that to explain the effects we produce we must seek the cause in the subjective experience of the convulsion and resulting interference in the patient's state of consciousness.

In 650 cases treated with electric convulsant therapy (E.C.T.) in Graylingwell Hospital, Chichester, extra- and intra-murally, it was observed that the best immediate results were achieved in those depressive episodes chosen from different nosological groups which showed the somatic accompaniments of depression, such as motor retardation, loss of weight, loss of turgor of the skin, and so forth. In these there is a common physical denominator.

In 132 cases of involuntional melancholia and 145 depressions with cyclothymic personality background, the conscious psychological reactions whilst undergoing electric convulsant therapy are, in comparison to other psychiatric conditions, significantly scanty. The answers he gives when the patient is asked about the treatment, and the views he expresses spontaneously in the ward to nurses and fellow patients, are remarkably few. The slight post-convulsion confusion is transient. The same type of memory defects which Brody has described in some patients after electric convulsant therapy lasting for months is noticeable during the confusional state. The recall of trivial occurrences is impaired, and there is some perplexity of spatial orientation, with particular reference to places where personal belongings have been left. This confusion is accompanied by complaints of headache, sickness, general malaise, organ sensations of numbness most frequently localized in the head, paræsthesias, giddiness. If the confusion is prolonged for more than a day or two, especially in involuntional melancholia, an underlying cerebral arteriosclerosis—the differential diagnosis of which is so difficult in the early cases—ought to be suspected. In the uncomplicated depressive states the post-convulsive bewilderment does not last longer than one to two hours, after which the patients report a marked relief of their original symptoms. This improvement, which only rarely swings over to overt hypomanic reactions, is not experienced—if not suggested extraneously—by the patient as being the direct result of the treatment. The underlying or concurrent deep emotional, instinctual conflicts are more successfully repressed only. To confront the “ego” with these conflicts after electric convulsant therapy in the psycho-analytical sense is dangerously likely to precipitate relapse into psychotic depression. Before the treatment any direct or indirect psychotherapy is impossible owing to the incapacity of the patient for transference. Psychiatric help in environmental adjustment is of supreme importance, however, after discharge from hospital or for out-patients.

The importance of the quality of the “group spirit” in the ward to which the patients go after treatment cannot be exaggerated; the positive suggestive influence of fellow patients who are on the way to recovery serves as an object lesson to others commencing treatment and does much to alleviate the dread or indefinable apprehension before each session. Despite the retrograde amnesia which covers the very short pre-convulsive aura

the index at a level of 1% or less; (c) particulars of all other measures taken to control the transmission of yellow fever within the area or its transmission outside; (d) any other information which might be of value to UNRRA in assessing the position.

In addition the Commission pointed out that areas within an endemic area may have to be reclassified from time to time and need no longer be considered endemic; when recognized, adequate, sustained control measures have been applied to eradicate mosquito vectors and to eliminate the conditions favouring the occurrence or spread of yellow fever. The Commission also placed on record the extent to which they had been impressed by the value of the eradication measures already carried out in certain parts of the Western Hemisphere. On the other hand, they stressed that failure to carry out such measures may lead to areas, previously considered to be non-endemic, being classified as "endemic areas".

The recommendations of the Quarantine Commission were duly accepted by the Central Committee on Health, and are now in process of being implemented by UNRRA.

To complete this outline of the 1944 Conventions it is necessary to point out that a clause in each Convention limits its duration to eighteen months from the date on which it came into force. Personally, I think the period is too short to obtain full knowledge of the working of the new provisions. Nevertheless, useful experience should be gained. Before the Conventions expire a formal International Conference is to be assembled to review the then position and draft new Conventions. Printed copies of the Conventions should soon be available but when they are studied it is well to bear in mind that International Conventions are not necessarily the opinions of one or even two sets of experts but are often a compromise between conflicting views. Delegates to Conferences have to concede some points and accept others if the largest measure of international agreement is to be reached.

To conclude this brief summary the following paragraph from McCallum's valuable review of International Hygiene [6] seems appropriate:

"A study of the Conventions which resulted from the International Sanitary Conferences of 1892, 1894, 1903, 1912 and 1926 shows an interesting development in the practical application of more recent epidemiological knowledge—the role of the rat and the flea in plague, of the mosquito in yellow fever, and the lessened importance attached to fomites. Furthermore, quarantine practice under the Conventions has gradually been revised so as to differentiate the measures, applicable for each disease, according to its mode of spread."

The Conventions of 1944 now carry the practical application of epidemiological knowledge a step further—the protection afforded by inoculations against yellow fever, recognition of the value of inoculations against typhus and the value of effective insecticides. An attempt is also made to meet the old difficulty of validity of medical certificates by including International forms which governments are asked to adopt.

Finally, it is interesting to speculate what epidemic catastrophes might arise, as the result of the present turmoil, if International Conventions and Agreements based on our epidemiological knowledge had not been drawn up for, according to Creighton [7], no single thing stands out more clearly as the stroke of Fate in bringing the ancient civilization to an end than the vast depopulations and solitude made by the plague which came with the corn-ships from Egypt to Byzantium in the year 543, during the reign of Justinian. The 1944 Conventions were prepared under considerable difficulties and it seems fair comment to state that they are a definite attempt to strengthen and adapt the existing Conventions in anticipation of some of the difficulties which may face the United Nations and that, unlike most of the earlier Conventions, their preparation has not waited until pestilence was in our ports, our docks or our cities.

On the successful conclusion of the first stage in international collaboration for the prevention of epidemics it will be agreed that UNRRA is much to be congratulated.

A discussion followed in which Sir Alexander Macgregor, Dr. Leavell, Dr. J. A. H. Brincker, Dr. I. Corbett and Dr. Melville Mackenzie took part.

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The subjective experiences of schizophrenics to E.C.T. are very difficult to assess; clinically the affective part of their condition only is changed—that is if they are depressed. The hallucinatory experiences remain unchanged after a short period of lesser intensity. It has no effect whatsoever on the schizophrenic thought disorder. Paraphrenics, and paranoid schizophrenics of late onset with preserved personality, quite frequently involve the E.C.T. in their delusions and persecutory apparatus.

The post-convulsive psychomotor automatism in psychoneurotics and psychopathic personalities is often extremely dramatic, and although apparently covered by complete amnesia, may express in a choreographic way repressed subconscious memory material.

This apparent "catharsis" does not help the psychoneurotic patient.

Coarse hysterical syndrome in primitive personalities, especially when malingering is superadded, responds well to the very powerful suggestion of E.C.T. paraphernalia, but they react in the same way to other similarly suggestive remedies.

The experiences in insulin treatment of kaleidoscopic perceptual changes after awakening from insulin comas have been described by Benedek, Schilder, Mayer-Gross, Sargant and Slater, and others. The patient's tendency to test reality after awakening follows the patterns of infantile libidinal development. One witnesses a short recapitulation from narcissistic libidinal cathexis to new object libido. The warmth and congruity of affect in nuclear schizophrenics successfully treated with insulin is not found after any other treatment, even leucotomy.

In leucotomy also, the conscious psychological experience of patients of different nosological categories to the treatment itself is marked by its relative absence. After the turmoil of cerebral shock, cortical irritation, hypomanic frontal lobe release phenomena, and other neuropathological sequelae are over, or compensated for, which is not until six months after the operation, the patient is sufficiently settled for one to ask him what he thinks and feels about it all. The most outstanding manifestation is that such a major operation in persons of well-preserved personality with average, or above average, intelligence, appears to be of much less subjective significance than, say, an appendix operation. (Patients with well-preserved personality with average intelligence numbered 40 among 120 followed up after six months. The total number of operated cases was 158.) This is in part due to the pre-operative lack of insight, but there are signs which suggest that in the body image the frontal lobes do not appear at all.

In the case of a physician, for example, the operation was fully discussed beforehand and his own permission obtained. He is suffering from paranoid schizophrenia but has no memory impairment at all and is of above average intelligence, and yet he is now quite incapable of giving a theory of what the operation is, except: "It was for the nerves, I suppose." He has no idea in which part of his brain the incisions were made. He also describes the following recurrent dream: He is in an arena where lions are going to be fed; he knows a piece of meat is going to be thrown to them; he is frightened and walks away. Before operation this dream had the quality of a nightmare and he awakened shouting. Now, eight months after the operation it has lost the frightening qualities—he reports "the lions are tame now and playful," but he still has to walk away before the meat is thrown.

This patient is rather an exception to the rule: more than 80% among the 120 in whom these observations were made, had no dream life at all after the operation, or a greatly diminished one. They report also in decided terms the entire lack of daydreaming since they had the operation. A submissive, over-polite attitude is most noticeable in patients over 55 (22 of our cases), but it is seen in more or less marked degree in all who recovered. The tiredness, especially of the eyes, about which so many patients complain, more than six months after the operation, is actually not physical but is meant to express a diminished mental vigilance, as careful psychiatric investigation revealed.

The clinical results of leucotomy are the content of another paper.

[I gratefully acknowledge the advice and criticism of Dr. Carse, Medical Superintendent of Graylingwell Hospital.]

Excerpts of case records were read, two of which are appended:

M. V., male, aged 26, out-patient, suffering from anxiety hysteria with depressive features, virtually wanted to gouge out his left eye immediately after the fit was over; two nurses had to restrain him.

As his condition did not improve after four E.C.T. treatments he was taken over from

MAY—PSYCH. 2

in E.C.T., all patients have a feeling of apprehension. Mayer-Gross in his paper on retrograde amnesia in E.C.T. found this, for memorized material, to last a minute before the fit. What do the patients, without exception, dread then, as the phase of post-convulsive psychomotor automatism is also not consciously remembered? I think it is the violent and sudden interference with the state of consciousness, plus a memory of the id for the convulsion itself. The intensity of the fear reaction is individual and obviously dependent on diverse personality factors; it has, however, a meaningful relation to clinical types. In involuntional depression, endogenous melancholia, except agitated forms, the apprehension caused is markedly less than in psychoneuroses, whether with convulsive or hysterical personality background. There is a fundamental difference in the experience of E.C.T. itself in melancholia which is not sufficiently explained by the therapeutic effect alone. Patients show a steady persistence in attending as out-patients and as in-patients complain but little, in remarkable contrast to patients with other types of mental illness. Explanation of this behaviour by the supposed subconscious self-punishing tendency and the gratification of death wishes towards the ego could not be confirmed. It was impossible to ascertain in the dream or phantasy life of these patients anything of that kind.

Neither the manifest nor latent dream content in melancholics shows any trace of elements which would in a valid way point to such a subjective meaning of the treatment. Dreams of a traumatic situation, such as a railway crash, drowning, fire, and similar catastrophes, which contain an element of replaced recapitulation compulsion for the experience of the fit itself, are complained of by psychoneurotics but not by melancholics. On the contrary, the restless sleep of the latter, so frequently interrupted by nightmares before treatment, soon, in the majority of our observed cases, changes into a healthy restful sleep after four to five major convulsions. Indeed, if this insomnia disturbed by nightmares persists, especially in involuntional melancholia, in spite of E.C.T., it ought to be considered, in our experience, as a first warning sign of cerebral arteriosclerosis or other organic deterioration, so often masked in involuntional states.

The post-convulsive psychomotor automatisms which we call in a purely arbitrary way "abreaction," by no means implying a cathartic effect of such phenomena, are also conspicuous by their relative absence in uncomplicated depression, in contrast again with psychoneurotics and allied personality disorders. A startle reaction occurs, however, when approached immediately after regaining consciousness without exception in all cases. The most usual report in depressives after four to five treatments is "I feel as if a tight band round my head has been removed, all my previous fears and feelings of hopelessness seem to be so remote—but I don't like the treatment very much, how many more must I have?"

In expressing appreciation for the help so rendered, a lack of affect is almost invariably present, and if the course of E.C.T. has reached about fifteen to twenty sessions, a plateau type of over-politeness is noticeable which is emotionally shallow and insincere. If asked about this they give thanks again but are not indignant, and they are at a loss to explain this behaviour. This feature is the more striking as at the same time the patients are most emphatic in saying that they have regained self-confidence to face life. This over-politeness is due to a diminution of self-assertive drive, and to a fading of colour and blunting of the edge of the personality. This is shared, but is much more pronounced, in cases after leucotomy, organic deterioration, in severe idiopathic epilepsy and malaria-cured G.P.I.s. After prolonged E.C.T. the individual uniqueness of the ego becomes veiled also: the difference is, in comparison to irreparable organic damage, that the specificity of the personality returns after the termination of the treatment. In about two months this numbing effect on the ego disappears.

The Rorschach test in patients receiving over 15 fits, as tested in 50 cases, shows in persons with otherwise average intelligence a particular poverty in good F. and W., and a prevalence of Dd, of 1 or 2% bad form, with a tendency to perseverate and to reject. Kinæsthetic whole responses are markedly absent.

Agitated depression and hallucinatory excitements, stupor states, with refusal to take food, respond very much better to cardiazol fits. The remarkable sedative effect of pharmacological convulsions was pointed out to me by Carse, and in 74 observed cases out of a total of 86 of that group the advantage over E.C.T. was graphically demonstrated. Whether this is due to the psychological effect of the agony of experiencing the comparatively long pre-convulsive aura, or in a topically different onset of epileptic discharge in the brain, was not within our resources to decide. The findings of Parfitt, Schilder, Silbermann, and others, regarding the experience of cardiazol, fits are shared by all who make use of this treatment. A pre-convulsive aura of annihilation in cardiazol is remembered by patients as lasting endlessly, whereas its objective time is from fifteen to thirty seconds.

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S., M.R.C.O.G.

[February 16, 1945]

THREE CASES BY BRAITHWAITE RICKFORD, M.D., F.R.C.S., M.R.C.O.G.

Sarcoma of Cervix.

Mrs. H., aged 54.

History.—First seen 6.5.42 complaining of a blood-stained vaginal discharge for five weeks. Her previous health had always been good. She had had five children without any complications, the last being sixteen years ago. The periods had always been normal, starting at the age of 14, and finishing at the age of 40 when she had had a simple mucous cervical polyp removed. Following this, normal menopause had occurred.

The discharge had started suddenly five weeks ago. It was profuse, yellow, offensive and blood-stained. There had been some backache for the previous week, which was worse on exercise and relieved by rest. There had also been some anorexia and malaise for a fortnight. There had been no upset of bladder or bowel functions.

On examination under an anæsthetic on 1.6.42, a brittle, friable growth of the cervix was felt. The uterus was normal in size, but there was very little mobility, and the parametria on both sides were thickened. On inspection, there was a necrotic cervical tumour to be seen.

50 mg. of radium were inserted into the uterus and left for forty-eight hours, after removing a piece of the growth for biopsy.

Pathological report (Dr. Bamforth): Sarcoma of the cervix with a number of giant cells and some hyperchromatic nuclei.

Following the insertion of radium there was a slight pyrexial reaction for two or three days. Three weeks later radium was again inserted, using the same dosage. It was noted at that time that the growth involved the whole cervix, that there was no ulceration, and that the tumour felt like a mass of boiled tapioca. The patient was discharged ten days later without any further reaction.

21.7.42: On examination, the cervix showed many grape-like polypoidal nodules. Two months later there was no change.

12.1.43: The cervix now showed a transverse scar with one small cystic nodule about the size of a pea. The patient had gained 2 st. in weight since May 1942.

3.10.44: The patient was extremely well. She noticed no abnormal symptoms and there was no evidence of any recurrence.

This case has been reported to show the reaction of a sarcoma of the cervix to simple irradiation.

My thanks are due to Mr. James Wyatt, under whose care this patient was admitted, for permission to publish this report.

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a colleague for psychotherapeutic sessions. His main symptoms were a disabling fear of fainting in public, giddiness, claustrophobia, fear of sickness in buses and trams. He could not work because of these. The free associations revealed, among other things, that he suffered during adolescence from migraine, mostly on the left side. He was neurologically examined at Queen Square Hospital—N.A.D. Ophthalmologically: uncomplicated hypermetropia of three diopters on both sides.

In one session he related a dream in which he was chased by a monstrous sea animal with one eye, and awakened with intense anxiety. Associations to this dream let him remember an episode when aged 6. He was gambolling on the beach and was struck in the left eye with a pebble by a playmate. He was extremely frightened then, the blood running from his eye, as he thought. At the same time, when about 6, but before this occurrence, his awakening infantile sex curiosity and play were suddenly interrupted when once discovered by his mother, who threatened him with blindness if he did, or looked at, "such things" again. When as a small boy he was hit in the eye, he already fantasied it as a punishment for his instinctual urges.

This description of a patient who had been in Graylingwell Hospital, Chichester, for thirteen years, suffering from chronic manic-depressive psychosis and is now socially recovered, is typical:

E. D. C., female, aged 50 (leucotomy 29.4.43). Interviewed 8.11.44. On asking her about the operation she stated: "It is marvellous to have the peace of spirit after so many years of illness." Objectively, this seeming insight is, however, shallow and accompanied by constant expression of thanks in a monotonous and over-polite manner. Her face is expressionless, rather empty. She has no complaints, apart from the subjective feeling of slowing down in her general reactions. At the same time, she does all the shopping for the family of four, and keeps the house tidy.

Dr. W. Mayer-Gross: Dr. Frank's observations are not only of great theoretical interest, but also a contribution to the important new tasks which psychotherapy has to face after the introduction of the new physical treatment methods. They cannot be practised in a psychological vacuum. Speaking in terms of psychopathology, convulsion and insulin therapy as well as leucotomy produce a transient regression, each in another time pattern and probably on different levels. In hours or days they open up instinctive strata and layers of the unconscious into which psychoanalysis takes weeks to penetrate; and this in patients inaccessible to psychotherapeutic methods otherwise. Everybody applying these therapies realizes the importance of favourable environmental influences and of many other psychological factors for the final result. This seems to offer a promising field for systematic psychotherapy of hospital patients.

Dr. L. C. Cook recalled that in the early days of convulsive treatment the charge was repeatedly made against it that its effects were solely due to the unpleasantness and fear it engendered; it was likened to the swinging bed, the wire brush and other outmoded methods of treating hysterics. For this reason he had tried to find out whether the results of convulsive treatment in the first 275 patients treated at Bexley Hospital supported this view. These early cases were treated with cardiazol which gave ample opportunity for fear to exert its reactions. Any personal bias in evaluating results was practically eliminated by the fact that the assessment of the degree of fear was made by the nursing staff who had no idea why the information was required, and that the therapeutic results in all but a few of the most recent cases had already been assessed before this investigation was thought of. The figures showed unmistakably that patients exhibiting the greater degrees of fear did not tend to do any better, in fact they did less well than those exhibiting only a normal amount of dislike of the procedure. Similar experiments on a smaller scale had led American workers to the same conclusion, and further confirmation came from the use of E.C.T., which produced far less apprehension, but very similar results.

This investigation, of course, dealt only with overt manifestations of fear. The psychological effect of being plunged into sudden unconsciousness and the identification of this unconsciousness with death had been taken by some workers as the basis of any improvement achieved. Schilder, for example, had pointed out the friendliness of patients in the post-convulsive state, even when still confused, and considered this to be due to previous libido-fixations having lost their importance, resulting in renewed interest in people nearby. If this were true one would have expected any method of inducing repeated rapid lapses into unconsciousness to have a similar effect, but it was well known that courses of nitrous oxide anaesthesia, amytal, &c., were not nearly so effective as convulsions.

Flescher had rejected the fear motive but had formulated an interpretation based on Freud's theory that melancholy after the loss of a dear one depends on a strongly ambivalent attitude towards that person. The lost object is identified with the ego, and aggressiveness, previously unconscious, is directed against it in the form of guilt feelings, self-depreciation, self-destructiveness, &c. The fit discharges large amounts of energy inherent in the destructive and death drives and unloads them in an individually and socially harmless manner. Such an interpretation was not unattractive and was difficult to disprove, but it was not easily applied to a good many cases that had done well with convulsion therapy. He (the speaker) thought it more probable that mechanisms dependent on chemical or structural changes were the significant factors, both in the production and in the alleviation of symptoms in the so-called biogenetic psychoses.

last year. There had been two children without any abnormalities, the last thirty-two years ago. One miscarriage had occurred which had required evacuation of the uterus.

A heavy vaginal discharge had been present for two months which required two to four diapers a day. It was rather thick, whitish in colour, and often definitely pink-stained. There had never been any frank bleeding, and it had never been offensive. There was no pruritus, pain or discomfort anywhere. She was feeling very well in herself, there had been no loss of weight or anorexia. The bladder and renal functions were normal.

On examination.—Healthy, average weight, not anæmic. Abdomen normal. On vaginal examination the cervix was small and atrophic, and a firm mass could be felt in the left posterior quadrant of the pelvis and was thought to originate from the uterus. 29.8.44: The cervix was dilated and the uterus measured only 2 in. No curettings were obtained. Following this there was slight pyrexia associated with some lower abdominal pain for three weeks.

3.11.44: Laparotomy. No free fluid in the abdomen; a tumour about the size of a grapefruit was found in the left posterior quadrant of the pelvis which was adherent to the back of the uterus. It was found that the upper serous covering of the tumour was the grossly thinned wall of the distended left fallopian tube. The tumour had dilated the abdominal ostium and was attached directly to the posterior surface of this broad ligament and the uterus. It was removed in one piece with the tube. A considerable area of ragged, oozing tissue remained in the tumour bed. The abdomen was closed with a drain down to the pelvis. The left ovary was seen to be small and atrophic after the growth had been removed, while the right appendages were normal and the uterus was small and atrophic. No glandular involvement was found, and the omentum was free from secondaries, as was also the liver. The tumour after removal was brain-like in appearance. There were considerable areas of necrosis and hæmorrhage with many small cystic spaces. The fallopian tube was grossly dilated in its upper two-thirds, with the tumour growing from its inner wall and through the abdominal ostium.

Convalescence was complicated by a small infarct of the lung sixteen days later, which rapidly resolved. A full course of deep X-ray treatment was given to the left side of the pelvis.

10.2.45: Patient very well; no abnormality in the pelvis.

Pathology (Dr. Bamforth): Spindle-cell sarcoma arising from the wall of the fallopian tube.

The first reported case of sarcoma of the fallopian tube was described by Sanger in 1886, and the most recent review of the literature is by Jorgensen (*Acta. obstet. gynec. scand.*, 1938, 18, 326). He reviews sixteen cases in all, the only previous English reference being by J. B. Banister, *Proc. R. Soc. Med.*, 1924, 17, Sect. Obstet., 31.

My thanks are due to Mr. A. J. Wrigley, under whose care these last two patients were admitted, for permission to publish these reports.

TWO CASES BY JOHN P. ERSKINE, B.Sc., M.B., Ch.B., M.R.C.O.G.

Grossesse Extramembraneuse.

The patient, aged 30 and pregnant for the fourth time, took quinine pills and douched repeatedly in the hope of producing abortion. As a result the membranes ruptured at 18½ weeks, and she discharged clear fluid intermittently *per vaginam* throughout the rest of the pregnancy. The condition was confirmed by analysis of the fluid which was found to be liquor amnii. Fœtal movements were never felt, but the fœtal heart could be clearly heard.

The pregnancy terminated spontaneously at 35 weeks in the birth of a living female child weighing 4 lb. It died shortly after birth and was found to have multiple deformities, bilateral talipes, subluxation of the right knee, and soft tissue contractures at both elbows. The placenta was of the circumvallate variety.

An Unusual Ectopic Pregnancy.

Presacral sympathectomy was performed for severe spasmodic dysmenorrhœa accompanied by epileptiform convulsions. Three weeks after discharge from hospital the

Primary Carcinoma of Fallopian Tube.

Mrs. L., aged 36, was first seen on October 25, 1944, complaining of sterility. Twenty-four years previously she had had an acute appendicitis with a pelvic abscess, which had necessitated her being in hospital for nine months. She had been married for six years, her husband had been at home throughout and on investigation had been found to be fertile.

Her menstrual history was quite normal, starting at the age of 15, and was regular. She had noticed some vaginal discharge for the previous ten years, which was most marked for the seven days following menstruation.

On examination she was a healthy patient, not anæmic, and was of average weight. The abdomen showed a firm tumour in the mid-line, reaching about 1 in. above the symphysis pubis. It arose from the pelvis and was slightly mobile. Otherwise there was nothing of note on abdominal examination. Vaginal examination showed that this tumour was in the uterus, which was regularly enlarged to the size of about a fourteen weeks' pregnancy. It was hard in consistency and mobility was limited. To the right of the uterus and posteriorly was another tumour, which was rather softer and apparently attached to the uterus.

Laparotomy was performed following an unsuccessful attempt at insufflation. The intestines were thickly adherent to each other and to the pelvic organs, with dense matted felty adhesions. It was impossible to recognize the uterus or appendages on inspection. The uterus, however, was palpated and found to contain a hard tumour in the anterior wall. To the right of the uterus was a softer mass, which appeared through the adhesions to be of a bluish-brown colour, rather resembling that of a tubal abortion. This mass was separated digitally and during this process a friable papilliferous mass, the size of a golf ball, fell out of the tubal orifice. Surrounding the mass was a collection of thick, blood-stained glairy mucus. The right tube was then removed, the ovary being left *in situ*, and apparently normal. The left adnexæ were palpated through the adhesions and were apparently normal. A myomectomy was then carried out for an interstitial fibroid after dissecting blindly through the adhesions covering the anterior wall of the uterus. Hæmostasis was not absolute and the abdomen was closed with a tube drain for forty-eight hours.

Convalescence was uneventful and a full course of deep X-ray treatment to the right posterior quadrant of the pelvis was instituted sixteen days later and completed in twenty-eight days.

Four months later the patient was extremely well and pelvic examination revealed no abnormality. Menstruation had occurred once since operation.

Pathology (Dr. Bamforth): "Papillary-columnar-cell carcinoma of the fallopian tube."

Orthmann, in 1886, reported the first authenticated case of primary carcinoma of the fallopian tube, though Doran, in 1896, mentioned an unreported case of Raynaud's from 1847, while in 1861, Rokitsansky gave the first pathological description of this disease.

Cases have been reported before this Society more recently by Mr. A. J. Wrigley in 1926 and by Miss Alice Bloomfield in 1936 (*Proc. R. Soc. Med.*, 30, 52).

The most recent review is by H. J. Baron (*Canad. med. Ass. J.*, 1940, 43, 118-121), when he brought the total number of cases to 363, since when I have been able to find a further 15 in the literature. This disease is most common between the ages of 40 and 55, though cases have occurred in a girl of 18 and a patient of 73.

Symptoms are few, the most important being a slight watery, sometimes pink-stained, discharge. This may occur at intervals and is associated with attacks of colicky low abdominal pain, when the distended tube may empty its contents into the uterus.

The diagnosis has only been made pre-operatively on one occasion. However, the combination of a discharge of that character without uterine abnormality but accompanied by an adnexal enlargement, might suggest a tubal carcinoma.

Primary Sarcoma of Fallopian Tube.

Mrs. C., aged 69. 16.8.44: Complained of vaginal discharge for two months. The previous history was not significant. Menstruation had started at 15 and had always been normal. The menopause had occurred nineteen years ago when menstruation ceased suddenly and there had been no further loss or discharge until the onset

that these are decidual cells and that the picture is that of decidual reaction taking place in an ovarian endometrioma.

Family history.—These two patients are sisters. They have two brothers and two other sisters. The oldest member of the family is a sister aged 40 who has one child aged 17. There is another sister, Mrs. K., aged 36, who has one child aged 9 years, and who is anxious to have another. She also complains of severe backache. It seems possible that she, also, may have pelvic endometriosis.

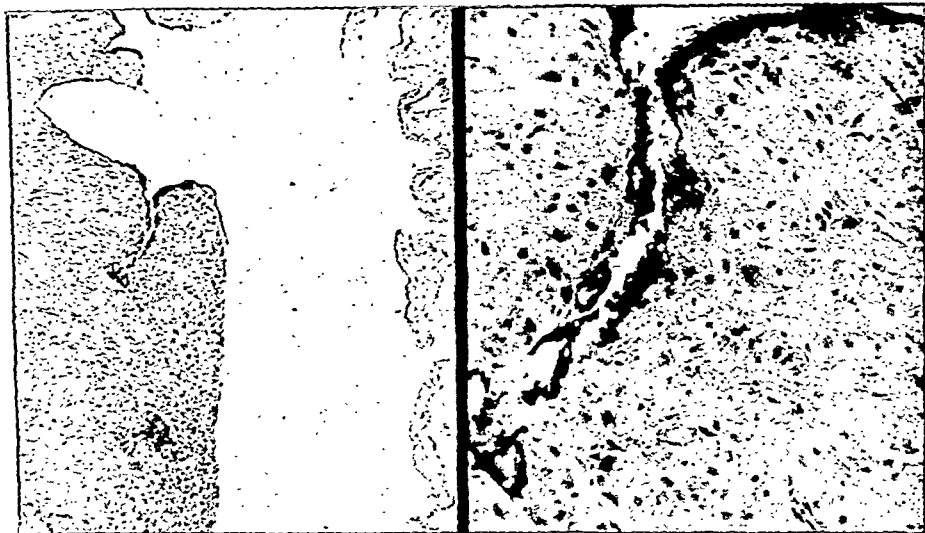


FIG. 1.

FIG. 2.

Cyst wall from Case II: (a) showing epithelial lining and formation of gland spaces. $\times 45$; (b) showing glands of endometrial type and stroma with decidual reaction. $\times 200$.

On examination Mrs. K. was found to have a normal uterus, but there was a round, mobile swelling, about 3 in. in diameter which seemed to be in the right ovary.

Comment.—The combination of ovarian endometriosis and pregnancy is a rare one. The first case seems to have been reported by Sampson in 1922. Scott (1944) was able to find only seven cases so far reported in the literature and he added a further two cases. The reason for the rarity of this combination is that pelvic endometriosis tends to be associated with sterility. This is probably due to the involvement of the ovaries, since Sampson (1927) showed that the tubes were patent in 284 out of 293 patients with endometriosis and adduces this fact as evidence in support of his implantation theory of the origin of the disease.

The occurrence of endometriosis in two members of the same family also seems to be rare and no report of a similar occurrence has been found in the literature.

Regarding the relation of pregnancy to endometriosis, it has been suggested by Sampson (1924) that pregnancy lessens the incidence of the disease, though he admits that this is difficult of statistical proof. He also suggests that pregnancy may cause regression of existing lesions. Cases have been observed where endometriosis of the recto-vaginal septum has complicated pregnancy. It has generally been found that the lesions tend to increase in size for the first half of pregnancy but in the later months they regress and cause no obstruction to natural delivery.

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patient was readmitted in a collapsed state, and at operation a ruptured primary 6-week abdominal pregnancy was found.

It is thought that the fertilized ovum must have been present in the fallopian tube or abdominal cavity when the first operation was performed. Implantation in the pouch of Douglas subsequently occurred and may have resulted from the accidental displacement of the ovum from the fallopian tube during resection of the presacral nerve.

Chocolate Cysts of the Ovary (Ovarian Endometriosis) and Pregnancy: A Report of Two Cases Occurring in Sisters.—JOSEPHINE BARNES, D.M., F.R.C.S., M.R.C.P., *First Assistant, Obstetric Unit, University College Hospital.*

CASE I.—Mrs. D., aged 33, primigravida. Admitted to the Obstetric Hospital, University College Hospital on April 22, 1944. Last menstrual period February 5 to 8. Complaining of dragging pain in the right side of the abdomen. Menstruation normal and regular 3/28.

On examination there appeared to be a soft, cystic mass which was palpable *per abdomen* in the right iliac fossa and also palpable bimanually. A small, cystic mass was palpable in the pouch of Douglas. The pain complained of became more severe and it was decided to perform laparotomy.

Operation was performed on April 25, the duration of the pregnancy being then 11 weeks and 3 days. The abdomen was opened through a mid-line, subumbilical incision. The mass felt *per abdomen* on the right side was found to be the pregnant uterus, containing a small fibroid at the left cornu and pushed up into the abdomen by a mass lying in the pouch of Douglas. When an attempt was made to explore this mass, a quantity of chocolate-coloured fluid escaped. This was found to be coming from a cyst, arising from the left ovary, about 6 in. in diameter and adherent to the anterior surface of the rectum. The left ovary also contained the corpus luteum of pregnancy. The right ovary was normal. The cyst was dissected away from the rectum and out of the ovary, leaving the corpus luteum undisturbed. The ovary was repaired and the abdomen closed. The post-operative course was uneventful. Heroin, grain 1/10, was given four-hourly for the first forty-eight hours. There was no vaginal hæmorrhage.

The patient was seen at intervals in the antenatal clinic and the pregnancy progressed normally. She left London at the time of the flying-bomb raids, and was delivered on November 12 by Cæsarean section, apparently on account of uterine inertia, though no details are available except that mother and child are now well.

CASE II.—Mrs. B., aged 30, primigravida. Admitted to the Obstetric Hospital, University College Hospital on November 15, 1944. She was referred on account of an abdominal swelling in association with a 16 weeks' pregnancy. The last menstrual period had occurred from July 24 to 29 and menstruation has been normal and regular and accompanied only by slight backache.

On examination of the abdomen, a swelling was felt, arising out of the pelvis, which felt like the pregnant uterus. There was a soft, cystic mass in the right iliac fossa.

Operation was performed on November 21, the duration of the pregnancy being then 17 weeks and 1 day. The abdomen was opened by a lower right paramedian incision. The pregnant uterus appeared normal. The right ovary was replaced by a rounded cyst, 5½ in. in diameter, adherent to the back of the right broad ligament. The left ovary and tube appeared normal. Right salpingo-oophorectomy was performed. The cyst ruptured during separation of the adhesions and chocolate-coloured fluid escaped. The abdomen was closed. The post-operative course was normal. Morphine was given after operation and papaveretum grain 1/3 every four hours for twenty-four hours. The patient has attended the antenatal clinic at regular intervals and the pregnancy is progressing normally and has now reached 30 weeks.

Specimen: The cyst removed from the first case was unfortunately destroyed and no sections were made. The specimen from the second case is shown. This consists of a thick-walled cyst 5½ in. in diameter. The outer surface is roughened where the adhesions were separated. Traces of old blood are seen on the inner surface.

Figs. 1 and 2 are sections of the cyst wall. These show a lining of cubical epithelium which in one place is continued into some rounded gland spaces. Beneath the epithelial layer is a thick layer of large and rather deeply stained cells. It is suggested

that these are decidual cells and that the picture is that of decidual reaction taking place in an ovarian endometrioma.

Family history.—These two patients are sisters. They have two brothers and two other sisters. The oldest member of the family is a sister aged 40 who has one child aged 17. There is another sister, Mrs. K., aged 36, who has one child aged 9 years, and who is anxious to have another. She also complains of severe backache. It seems possible that she, also, may have pelvic endometriosis.

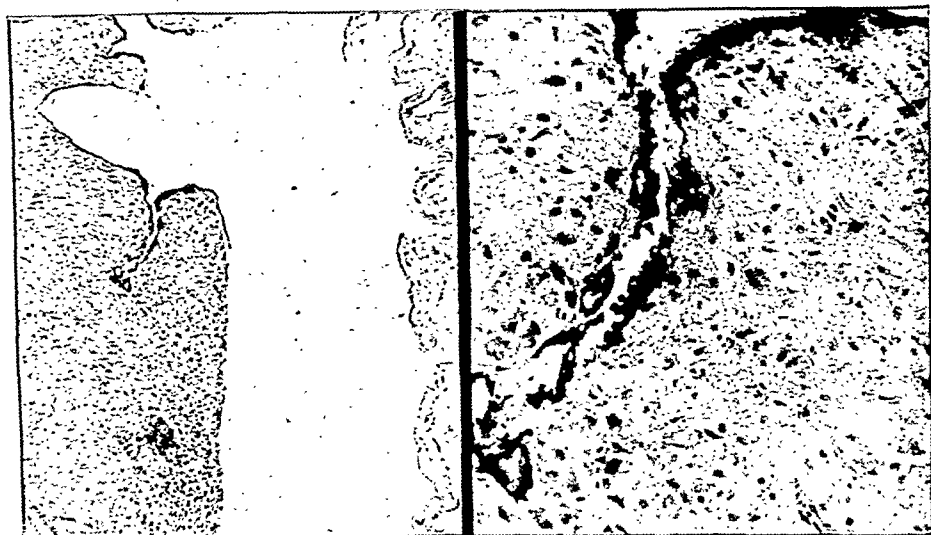


FIG. 1.

FIG. 2.

Cyst wall from Case II: (a) showing epithelial lining and formation of gland spaces. $\times 45$; (b) showing glands of endometrial type and stroma with decidual reaction. $\times 200$.

On examination Mrs. K. was found to have a normal uterus, but there was a round, mobile swelling, about 3 in. in diameter which seemed to be in the right ovary.

Comment.—The combination of ovarian endometriosis and pregnancy is a rare one. The first case seems to have been reported by Sampson in 1922. Scott (1944) was able to find only seven cases so far reported in the literature and he added a further two cases. The reason for the rarity of this combination is that pelvic endometriosis tends to be associated with sterility. This is probably due to the involvement of the ovaries, since Sampson (1927) showed that the tubes were patent in 284 out of 293 patients with endometriosis and adduces this fact as evidence in support of his implantation theory of the origin of the disease.

The occurrence of endometriosis in two members of the same family also seems to be rare and no report of a similar occurrence has been found in the literature.

Regarding the relation of pregnancy to endometriosis, it has been suggested by Sampson (1924) that pregnancy lessens the incidence of the disease, though he admits that this is difficult of statistical proof. He also suggests that pregnancy may cause regression of existing lesions. Cases have been observed where endometriosis of the recto-vaginal septum has complicated pregnancy. It has generally been found that the lesions tend to increase in size for the first half of pregnancy but in the later months they regress and cause no obstruction to natural delivery.

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TWO CASES BY JOYCE MORGAN, M.D.

Acromegaly with Pregnancy.

Primipara aged 34, married for seven years. Always suffered from headaches. Had not noticed any change in size of hands and feet, or in facial appearance. First seen at three months' pregnancy, with well-developed acromegaly. X-ray of skull showed enlargement of pituitary fossa, suggestive of moderate-sized pituitary tumour.

Acromegaly with pregnancy is uncommon because this disease is more frequently associated with atrophy of the ovaries.

Patient is now 36 weeks' pregnant, with no aggravation of symptoms.

Anæmia in a Rhesus-negative Woman during Pregnancy with a Rhesus-positive Fœtus.

This patient has had three successive pregnancies each associated with severe anæmia commencing at 36 weeks.

The first infant died of "a hæmorrhagic disease" but the other two were healthy, with no jaundice or anæmia.

In each case the onset of anæmia was followed in a few days by premature labour. Blood transfusion with Group O pool blood resulted in an increase in anæmia.

With the third pregnancy, hæmoglobin fell to 18% after blood transfusion, and was accompanied by jaundice, vomiting and pyrexia.

Examination of blood by Slough Transfusion Service showed it to be Group AII Rhesus-negative. The husband was Group OIV Rhesus-positive, and the baby was Rhesus-positive. Two pints of Rhesus-negative blood were given and the hæmoglobin rose immediately to 48% and continued to rise.

Anæmia in the Rhesus-negative mother with a Rhesus-positive infant has not been described but the repeated history of severe anæmia at 36 weeks in this case is suggestive.

Breech Presentation with Fracture of the Fœtal Neck: Recovery.—LINDSAY O. WATT, C.M., M.R.C.O.G.

A gravida 4 with a flat small pelvis was admitted as an emergency, well advanced in the second stage of labour, with a breech presentation. A Cæsarean section was considered inadvisable because of the mother's condition and the poor state of the fœtal heart sounds. Under a light anæsthetic the fœtus was delivered as far as the shoulders (with the arms out). However, the well-flexed fœtal head would not enter the brim of the pelvis. There was no room at the pelvic brim to allow the application of forceps, and the shoulders, by pressing against the perineum, held the fœtal head tightly jammed at the inlet through the taut fœtal neck. Repeated firm and sustained shoulder traction and pressure on the fœtal head *per abdomen* failed to force the baby's head into the pelvis. About a minute afterwards the cord stopped pulsating. Before decapitation was decided on, one last energetic pull on the fœtal shoulders with pressure on the fœtal head broke the baby's neck, and delivered the head. The cord was clamped and cut. The neck was very elongated and a finger could be placed posteriorly (by invaginating the skin of the neck) between the proximal and distal ends of the fractured cervical spine, at about the C.4 and 5 level. Traction had always been on shoulders kept at right angles to the A-P axis of the head.

The baby revived, and while tensing its muscles to cry, also contracted its neck muscles, reducing the spinal fracture spontaneously. A head, neck and chest cellona spica was applied which required renewing at three weeks. An Erb's palsy developed from the third to seventh day and disappeared entirely. (At the time of writing the child is eight weeks old, perfectly healthy and X-rays of the spine show no abnormality.)

The President stressed that the prevention of torsion of the neck was probably responsible for the child's survival, and that this principle should always be followed even in a very difficult breech delivery. He described the case as unique.

Ulceration of the Mouth Associated with Recurrent Ulceration of Vulva.—A. H. C. WALKER, M.R.C.S., L.R.C.P., D.R.C.O.G.

Girl, aged 18, has had recurrent ulceration of the mouth for the past eleven years, associated with recurrent ulceration of the vulva for the past eight years.

CASE REPORT

My patient, aged 18, was born in London and had never been abroad. Her parents, now dead, had spent many years in India and I have been unable to obtain other details of them. There are 3 healthy brothers and no history of similar lesions amongst her relations or friends. Her weight is $8\frac{1}{2}$ st., and her height is 5 ft. 4 in.

The ulceration of the mouth commenced at the age of 7, and of the vulva at the age of 11. Menarche was at the age of 14—her cycle being a four-day loss every four to six weeks, without dysmenorrhœa.

She states that the ulceration is preceded by a burning pain, and some erythema; then a gradual development of the ulcer; that she has no vaginal discharge, but a slight yellow, non-offensive discharge from the ulcer; that they never bleed; are slightly painful and frequently disturb her sleep.

The ulcer on the lower lip is of a shallow aphthous type—circular, with a marginal erythema, and there is no scarring.

Over the past ten weeks, I have been able to watch closely the development of the vulval ulcers; first the burning pain for twenty-four to thirty-six hours; associated with an erythema and finally a pustule around a hair follicle before the ulcer appears. This has an inflammatory halo; a yellow slough on the base; a circular outline (a large ulcer had a serpiginous outline); somewhat tender; non-punched-out edge; and no associated adenitis but gross vulval tissue loss and scarring.

The ætiology of this condition falls under three headings: (1) Infective. (2) Tuberculide. (3) Ovarian dysfunction or deficiency and secondary infection.

Investigations show that all systems are normal: Vaginal swab culture shows no pus, there are Döderlein bacilli and a very small growth of *Staph. albus* and *aureus* and diphtheroids. Swab from the ulcer shows *Staph. albus* and diphtheroids. No gonococcal or tubercle bacilli. Vitamin C in blood and urine are low but within the range of normal. Vitamin B₁ excretion is normal. Biopsy and smear show no Leishman-Donovan bodies or T.B. on sections to be shown. Guinea-pig inoculation suggested but considered to be of no value in view of biopsy and smear findings. Frei's test negative. Vaginal biopsy is normal.

Treatment.—Locally, orally or parenterally appears to be a failure.

In the literature, no specific pathological positive findings appear to be present. A few cases are reported to have improved with œstrogens—and to have been cured with injections of antuitrin-S but only so long as the injections are continued.

Pathology (Dr. Rogers): The slide shows an ulcerative type of lesion, the base of the ulcer consisting of granulation tissue covered with a thin layer of necrotic fibrin. Deep to this layer, the tissues are infiltrated with inflammatory cells, predominantly polymorphonuclear in type. This area also shows œdema, and, in the deeper portions of the lesion, there are numerous chronic inflammatory cells. Imbedded in the granulation tissue there are small numbers of nodular collections of cells—the periphery showing a number of mononuclear cells, but again in this circumscribed lesion the predominating cell is the polymorph. The centre shows necrosis with hæmorrhage. This picture is similar to the description given by Sutton for a lesion called Peradenitis Mucosa Necrotica Recurrens. One such case was shown at the Royal Society of Medicine in 1932 by Ravell (*Proc. R. Soc. Med.*, 25, 1739), and Gray recognized it to be of this type. A further case was shown in 1934 (*Proc. R. Soc. Med.*, 27, 1578, Sect. Obstet., 82). The clinical picture in my case, however, is different. She fits in better with the description for aphthous ulcers.

The tissues beneath the intact epidermis are replaced by hyalinized fibrous tissue, indicating that the process is long-standing. The vessels of the area show a marked degree of endarteritis obliterans.

The elastic stained preparation shows a breaking up of the elastic fibres, a finding one would expect in this type of inflammatory lesion. The Gram stain shows a remarkable absence of organisms—and no tubercle bacilli have been found after careful search of the Ziehl-Neelsen's slide.

This condition was first described by Neumann in 1895. Since then some 50 cases have been reported mainly in foreign literature—only 4 cases having been reported in America. Of these cases, 6 had a constant time relation to the menstrual cycle, as this case had. The ages were between 12 and 74—only 1 case and this patient occurring before the onset of menstruation.

The condition appears to be peculiar to women—but this is queried in an American paper.

[March 16, 1945]

Tuberculosis of the Cervix, Uterus and Appendages.—S. GORDON LUKER, F.R.C.O.G.

The specimen was removed from a 1-para aged 37.

The symptoms were those of increasing menorrhagia of a few months' duration. The last period lasted fourteen days. The patient was very anæmic. Panhysterectomy was performed on May 3, 1935, with removal of the right and left appendages. There was some pyrexia for the first week after the operation but the patient made a good recovery and the wound healed by first intention.

At the present time, nearly ten years later, the patient is still in good health.

The specimen showed a deep ulcer on the left side of the cervix uteri, the body of the uterus was enlarged with some small pale patches in the uterine wall. The fallopian tube on each side was enlarged and full of caseous material.

Comment.—This case was an example of pelvic tuberculosis limited to the pelvic organs and removed by operation with a satisfactory result and with no fresh occurrence of tuberculosis in any other system.

Mr. Gordon Luker agreed with the generally accepted doctrine that operations for pelvic tuberculosis were not free from risk and that in many cases the wound did not heal well and a permanent sinus resulted.

Another risk emphasized by Mr. Carnac Rivett was that miliary tuberculosis might follow radical operation.

Necrosis of the Liver and Massive Bilateral Suprarenal Hæmorrhage in a Puerperal Woman.—GLADYS H. DODDS, F.R.C.S.

Primigravida, aged 34, had a mild degree of toxæmia and was treated by reduced protein intake for ten days. Labour lasted twenty-four hours and a living child weighing 7 lb. was born spontaneously. Less than one drachm of trichlorethylene by Freedman's inhaler was used in the second stage of labour. The patient vomited frequently for thirty-six hours after delivery, was lethargic and had severe headaches. She became slightly jaundiced on second day. She had severe epigastric pain, a shivering attack and was comatose for about one hour on third day and died on fourth day.

Post-mortem findings.—Liver normal in size, uniformly yellow in colour with no hæmorrhages.

Microscopic examination: Massive necrosis involving many adjacent lobules and within these areas a few small clusters of surviving liver cells. Suprarenal glands were enlarged to three times their normal size, deep purplish in colour. There was extravasation of blood into cortex and small areas of focal necrosis. The other organs were normal and there was no evidence of sepsis.

The probable ætiology of this case of liver necrosis may be divided into (1) toxæmia, (2) low protein diet, and (3) trichlorethylene; there were no other deaths or mishaps from triline in the hospital at that time.

Torsion of the Pregnant Uterus.—DOUGLAS MACLEOD, M.S.

History.—Patient, aged 33, first seen in November 1943. One child aged 4. Last menstrual period was on September 13, 1943. General health good.

On examination the pregnancy was found to be complicated by an ovarian cyst lying in the hollow of the sacrum. It was decided to remove the cyst at the 16th week of pregnancy. She was seen again in January 1944. She complained of constant abdominal pain—of a dull aching character—and marked frequency of micturition. Her general condition was poor but most marked was the change in her mental outlook. She was extremely depressed, felt ill and was suffering from a severe degree of anxiety neurosis. It was decided to terminate the pregnancy at the time of removal of the ovarian cyst. Examination showed an abdominal swelling extending up to the level of the costal margin.

Laparotomy was performed on January 25, 1944, and the uterus was found to have rotated in a clockwise direction through 180 degrees so that the posterior surface was directly anterior. Lying behind the uterus and filling the pelvic cavity was a cyst of the left ovary. This was removed after the position of the uterus had been corrected. The uterus appeared quite normal in colour and there was no evidence of congestion, purple discoloration or hæmorrhages which are usually described. Hysterotomy was

performed for medical indications only, for there was no other reason, after the position of the uterus had been corrected, why the pregnancy should not have continued.

Comment.—The diagnosis of torsion of the uterus in pregnancy is rarely made, but in the cases reported, marked frequency of micturition is usually present together with a constant dull pain in the abdomen. This case is interesting because of the curious anxiety state induced and also though the torsion was through 180 degrees yet it was unassociated with any gross pathological changes.

THREE CASES BY ALBERT DAVIS, F.R.C.S.

I.—Rupture of the Symphysis Pubis.

Mrs. M. H., multigravida 2. First child is now 4 years old; spontaneous birth at term, weight 7 lb. 6 oz. Patient seen in August 1944, pregnant for the second time, due October 16. Examined and found obstetrically normal. X-ray examination 4.11.44 showed a normal pelvis. Forceps delivery was carried out on 9.11.44 at another hospital. There was apparently a good deal of difficulty on account of the large size of the infant (10 lb. 2 oz.). The patient awoke with extreme pain in the back and over the symphysis, and a dislocation of the latter was diagnosed and confirmed radiographically. The child was stillborn.

Subsequent progress followed radiographically shows that the original wide separation is somewhat decreased, and the left sacro-iliac dislocation is reduced. The patient walks with a waddle, and ambulation is particularly painful after rest. [Seven X-ray films were shown.]

II.—Symphyseal Osteo-arthritis.

Mrs. F. B., 32, gravida 1. Seen in second pregnancy at 24 weeks (29.7.44) complaining of pain over the pubis on walking. The disability rapidly increased in intensity and X-ray at 28 weeks showed a wide interval at the symphysis pubis. Tenderness was pronounced. Corseting relieved the condition adequately for six weeks, but after this time walking became impossible and the patient was completely bedridden, with uncontrollable pain over the pubis. Spontaneous delivery of a full-term normal child weighing 8 lb. 3 oz. took place on 28.11.44, with a tight binder applied throughout labour. There was some pubic pain in the first pregnancy, the baby weighed 8 lb. 8 oz. but there was no real disability. Subsequent progress has been good, she is symptomatically and radiographically improving and now walks quite well.

III.—Rupture of the Uterus Self-produced.

Mrs. J. B., 38, multipara 4. Admitted as emergency on 3.1.45 with the history that during an attempt to induce abortion by means of a syringe she had felt a violent pain in the abdomen of extreme intensity, at the moment she was injecting the contents of the syringe. She was nearly three months' pregnant, and had had some hæmorrhage that morning. Seen four hours after the injection she was collapsed and in great pain. Temp. 97°, pulse 110 and thready, colour good. There was some loss P.V., the abdomen was tense, not rigid but very tender all over. The signs of initial shock soon disappeared, but were rapidly replaced by those of internal hæmorrhage, and operation six hours later revealed an abdomen full of blood. This was scooped out and was found to contain the fetus in its sac, with the placenta, both lying quite free. The uterus was raised, to expose a perforation on the anterior wall high up, 2 cm. long, and bleeding freely. A rapid supravaginal hysterectomy was carried out with continuous blood transfusion, and the abdomen closed with interrupted silkworm sutures taking in all layers. (This rapid method of abdominal closure is ideal in these cases, and the scar seems to hold at least as well as the more orthodox layered one, and herniation is not more common.) The patient made a good recovery, except for an intra-abdominal abscess which had subsequently to be drained.

Comment.—Mr. Davis said that very careful questioning of a frank patient had convinced him that this was not a case of perforation by direct trauma, but of explosive rupture due to a forcible injection. There was a long clean hole too extensive and clear cut for a perforation, and absence of the mucosal protrusion which seems characteristic of the former (specimen shown). The fetus and placenta seem to have been literally blown out of the uterus rather than squeezed through the narrow rent by contraction.

Hydatidiform Mole with a 16 Weeks' Fœtus.—S. BANCROFT LIVINGSTON, M.B., B.S. (for W. RALPH WINTERTON, F.R.C.S.).

Mrs. G. P., aged 42. History of one miscarriage 1934, otherwise well.

On examination.—First seen 27.2.45 in the antenatal department. Last menstrual period 27.10.44. She had œdema of ankles, profuse albuminuria and a blood-pressure of 190/110. Her uterus was up to the umbilicus and was tender and soft. No fetal parts were distinguished.

Next day œdema up to the knees, urine boiled solid with albumin, blood-pressure 190/120. She was losing blood *per vaginam* and having rhythmical abdominal pains at half-hourly intervals.

X-ray of the abdomen: Fœtal parts seen. Approximately 16/52. Head not visualized. Blood-pressure remained at 180/110, albumin $2\frac{1}{2}$ parts per 1,000 (Esbach's), and she continued to have considerable œdema of the ankles.

Abdominal hysterotomy was performed on 3.3.45 under cyclopropane anaesthesia and a fœtus attached to a hydatidiform mole was removed. Post-operatively, her œdema settled completely in two days, her blood-pressure rapidly fell to 130/80 and has remained normal. Albumin fell to $\frac{1}{4}$ part per 1,000 (Esbach's) in three days, and two days later was unrecordable. Her plasma proteins have shown a steady post-operative increase. Blood urea has shown no significant change during her illness.

Pathology: Placenta showing hydatidiform degeneration, and, macroscopically, a fœtus of approximately 16 weeks attached. Microscopy confirmed the hydatidiform degeneration of the placenta.

Comment.—This case is of interest because of: (1) The severe degree of toxæmia associated with the 16 weeks' amenorrhœa. Brews states that only 35% of patients with hydatidiform moles show any albuminuria. (2) The markedly enlarged uterus, suspicious of hydatidiform mole, with fetal parts, visible on X-ray. (3) The presence of a normal 16 weeks' fœtus with almost complete degeneration of the placenta. Brews records 100 cases of hydatidiform moles; of these, 97 showed complete molar degeneration with no evidence of a fœtus, 2 showed a normal fœtus with hydatidiform degeneration of a twin, and only one showed marked vesicular degeneration of the placenta with a normal fœtus.

Three Cases of Solid Tumours of Ovary.—R. KELSON FORD, M.D.

I.—Papillary Cystic Carcinoma.

Patient, aged 61, one child. Increasing abdominal pain, nausea and vomiting for two years. Latterly, uterine hæmorrhage, pallor and weakness. At operation, thickly blood-stained fluid found; recent adhesions separated, and large, friable, partly cystic swelling of left ovary (removed). The patient was unwilling to accept radiotherapy. Three months later, her pelvis was full of growth, and death occurred two months later still.

Areas of necrosis and of purulent infiltration could be seen.

II.—Granulosa-cell Carcinoma.

Patient, aged 51, four children. Menstruation had ceased two years previously, but continuous loss had commenced three to four months before admission. At operation, there was a left simple epioophoric cyst in addition to the right tumour, which was of the "irregular" type. Radiotherapy was instituted, and she was certainly quite well a year later.

III.—Papillomatous Adenoma.

Patient, aged 49, five children. Menstruation was regular till some three weeks before admission, when loss became almost continuous. No other symptoms. At operation, a left tubo-ovarian abscess was found, in addition to this growth of the right ovary, the interior of which shows a few small cysts, while the free surface displays an exuberant papilloma.

Retroperitoneal Hæmorrhage Causing Death in a Woman near Term.—MEAVE KENNY, F.R.C.O.G., and I. DONIACH, M.D.

Patient, aged 30, second pregnancy, with hypertension and œdema appearing at 36th week; died within two hours of onset of severe abdominal pain and collapse following sexual intercourse. Laparotomy for post-mortem Cæsarean section showed massive retroperitoneal hæmorrhage in left half of abdomen, origin not discoverable. The uterus was normal. Early eclamptic changes in liver and kidneys also present and small subendocardial hæmorrhages.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[January 18, 1945]

Case of Multiple Minute Fibro-angiomata of Face and Ears (Pringle's Disease, Darier's type).—A. C. ROXBURGH, M.D.

J. T., male, aged 44. Has had for ten years very numerous tiny pearly tumours about 1 to 2 mm. in diameter scattered all over the sides of neck, upper eyelids, nose, cheeks and ears, being most numerous on the lobes of the ears and on the backs of the ears. On the face they are flat, on the ears they project. The tumours were first noticed ten years ago on the ears, but patient thinks they have increased in size and number in the last three to four months and are still increasing.

Family history.—No similar lesions in parents or in brother and sister. Patient is not married.

Personal history.—Had a great deal of acne on the back of the neck and head in the past but not active in the last five to six years. However he still has many blackheads and scars.



Multiple minute fibro-angiomata of face and ears.

Other skin lesions.—Has three to four de Morgan's spots near left nipple, two to three small brown flat pigmented moles on back. Has a small (1 cm.) flat brownish-red lesion on inner side of each ankle of recent development. No other skin lesions.

Section consists of solid whorls of fibrous tissue with some dilated vessels reminiscent of the cases of so-called Pringle's disease shown at this Section by Drs. Bamber and Freudenthal on December 22, 1938 (*Brit. J. Derm.*, 1939, 51, 174), in a woman of 50 in whom they first appeared at the age of 36 and by Drs. Twiston Davies and Freudenthal on May 18, 1939 (*Brit. J. Derm.*, 1939, 51, 482), in a woman of 49 in whom they first appeared at the age of 45. In Dr. Bamber's case the lesions were white but in Dr.

Twiston Davies' case they were red and vascular and bothered the patient by bleeding. I do not think that either of these patients had the lesions on the ears.

Dr. W. Freudenthal: Sections of one of the small tumours show a fibrous or fibromatous tissue with a marked angiomatous component. At some places the connective tissue is concentrically arranged around the vessels. I think the histology would be consistent with Darier's so-called forme fibroangiomateuse of Pringle's disease. The histological picture is not characteristic enough for me to make the diagnosis on histological grounds only, as I was able to in Bamber's and Twiston Davies' cases. I have not previously heard of lesions on the ears in Pringle's disease, nevertheless, I cannot think of a better classification.

Dr. A. M. H. Gray: So far as treatment is concerned, it might be worth while trying diathermy to one of the lesions and see the effect. As to the name of the condition, I think it would be wise to retain the name "Pringle's disease" as a clinical entity rather than a pathological one.

Dr. A. C. Roxburgh: Diathermy applied to a condition already fibromatous is not likely, I suppose, to make it keloidal?

Dr. A. Burrows: The use of the cautery point is much better than ordinary diathermy, being much more under control.

? **Morphœa with Tuberculous Histology: ? Necrobiosis Lipoidica** (Sections shown by Dr. FREUDENTHAL).—Captain G. LESLIE, R.A.M.C.

This man came along five weeks ago, having been sent by his medical officer on account of patches on the shin which broke down easily and ulcerated. The man is 30 years of age and there is nothing noteworthy in his family medical history. He has served in Egypt and Palestine. The first time he became aware of the condition was in 1941, when he felt two or three nodules on the legs, and applied medicaments to them himself, without any advice from his medical officer. The nodules gradually became red in colour and coalesced to form a plaque in the front of the shin. Fresh nodules developed just beyond the margin and they in turn became reddish in colour and coalesced and joined up with the original plaque. In this way the lesions spread until they reached the stage that members have seen this afternoon. The man also noticed that exercise caused the lesions to be painful, and particularly in hot weather they were irritable.

At present there is a symmetrical, sharply defined patch on the middle of each shin across the tibia. The shape is roughly triangular, being 6 in. by 2½ in. at the base. Its edge is 1 mm. raised above the surrounding normal skin, the central area seems slightly atrophic and is traversed by a number of telangiectases. The colour is a dull red, containing in some places a yellow tinge. The consistency is hard, the surface smooth, but shows a few grooves, apparently the remains of previous small ulcers; hair is absent. On the whole, the appearance is reminiscent of morphœa.

The man has seen various dermatologists and his case was demonstrated as morphœa at two dermatological societies in the North of England. Various tests show nothing abnormal. The blood and urine were normal. The Mantoux test was negative with a high dilution, but on a second test, with a concentrated solution, the result was positive.

W.R. and Kahn tests were negative.

X-ray examination of the chest, abdomen and bones revealed no tubercular focus.

Dr. W. Freudenthal: I excised a small outlying nodule on the left shin of only a few weeks' duration, representing the earliest stage of the condition. It was reddish, round, about 8 mm. across and formed by a firm infiltrate which clinically seemed to involve the upper part of the cutis; the horny layer was thickened.

Histologically, the epidermis is normal apart from some hyperkeratosis and flattening of the rete pegs. The cutis in its full depth, including some tela subcutanea, is transformed into a peculiar granulation tissue. Numerous strands of varying width consisting of fibrocytes, fibroblasts, masses of epithelioid cells and a few giant cells of the Langhans' type surround oval, round, or irregularly-shaped islands of condensed connective tissue, staining pale pink with eosin. A few round foci of densely aggregated lymphocytes are present. The elastic fibres are diminished in the connective tissue islands and are absent within the strands of tuberculoid infiltrate. No lipoids could be found in frozen sections.

It is difficult to make a diagnosis in this unusual case. Combining the clinical with the histological picture, I think this may be an instance of "morphœa with tuberculous histology" of W. N. Goldsmith. Like him, I am inclined to look upon this condition as related to necrobiosis lipoidica (see also Dr. W. N. Goldsmith's remarks on Dr. H. C. Semon's case, *Proc. R. Soc. Med.*, 1944, 37, 648).

POSTSCRIPT (Meeting 15.2.45).—A second biopsy, representing the later stage, was made over the edge of the large, hard plaque on the right shin, including an area showing a yellow tinge.

The histological picture is very much like that in the first biopsy, except that the connective tissue islands are smaller and the strands of tuberculoid infiltrate are wider with a larger number of giant cells. Here, about two-thirds of the lesion is formed by the infiltrate and one-third by connective tissue; in the first biopsy the areas covered by each were about equal. A large number of frozen sections were examined for lipoids, but with completely negative result.

Dr. H. J. Wallace: About eighteen months ago (*Proc. R. Soc. Med.*, 1944, 37, 149) I showed two patients with lesions of similar clinical appearance and which microscopically did show the fatty change. The first was a woman, aged 38, who had had lesions on the front of the shins for eight or nine years. These had been gradually progressing and, indeed, they still continue to progress in spite of all forms of treatment. She had a very strong family history of tuberculosis: she was the only member of quite a large family who had not died from tuberculosis before the age of 40. All the tests for tubercle were negative and her general health has been well-maintained throughout. The lesions strongly resemble those shown in the patient now under consideration.

The second patient was a girl aged 19, who showed much the same picture, but the condition was of much shorter duration—some few months only. No treatment was given beyond local occlusive dressings. The histological picture was characteristic of necrobiosis lipoidica, and the lesions resolved in less than a year. Both these patients had a guinea-pig inoculation of the biopsy material for tuberculosis with a negative result. Clinically I thought that the lesions of the patient shown to-day were typical of lipid necrobiosis. Histologically, whilst fat was not demonstrated in the section, the general appearances were, I thought, quite comparable.

Dr. W. N. Goldsmith: Unfortunately I did not see this case, but the description strongly reminds me of the case I showed here in 1929 (*Brit. J. Derm.*, 41, 226) under the title of "Clinical Morphœa with Tuberculous Histology". Since then I have several times suggested that it may be related to necrobiosis lipoidica.

Dr. A. M. H. Gray: It struck me that this case was extraordinarily like the case shown by Dr. Goldsmith. I agree with what he has said. We are dealing with a peculiar type of change in the skin. Some of these cases appear to start as granulomata, which may be produced by bacterial activity or chemical changes in the blood; in others no pre-existing inflammatory process is seen. There is some chemical process going on in the skin, whether originating in bacteria or not, which manifests itself as a sclerodermatous lesion. By observing a number of such cases, we may be able to group them better.

Mucin in Granuloma Annulare (with the exhibition of 54 slides and 2 coloured photomicrographs).—W. FREUDENTHAL, M.D.

My demonstration intends to draw attention and to confirm the findings of mucin in granuloma annulare by Prunty and Montgomery (*Arch. Derm. Syph., Chicago*, 1942, 46, 394). This substance had occasionally been seen by previous observers, but Prunty and Montgomery in their valuable paper are the first to have realized its significance and to have made a full study of it.

I had noticed mucin in two cases at Jadassohn's Clinic in 1925, and afterwards examined every case of granuloma annulare for it. In 1933 when I had to leave the Clinic, I managed to take the sections with me, but had to leave my records behind. The metachromatic stains faded quickly, two coloured photomicrographs which I had taken were unsatisfactory, so I felt unable to publish my findings.

The result of these investigations, in brief, was as follows: 29 cases of granuloma annulare were examined, 24 of them showed mucin. In three of them 2 biopsies were made, both were mucin-positive. In 5 cases mucin was absent. In London I examined 7 more cases, 3 were positive, the other 4 were negative. These cases mostly date back to a time when I could not personally control the technique, so, I am afraid, not too much reliance can be placed on these four negative findings.

The best results were obtained with thionin, according to Hoyer (cresyl-violet was nearly as good, mucicarmin in my material (mostly alcohol-fixed) proved unsatisfactory. Mucin in granuloma annulare is chiefly present in the foci of more or less altered connective tissue around which the infiltrate is arranged. Usually only one or two foci in the section show mucin, the others being void of it. The amount varies considerably, from traces to large masses.

As an illustration I am demonstrating sections from two cases. The first, stained with thionin, shows one focus containing a dense network of mucin; the pink area is almost large enough to be visible to the naked eye. In the second, though clinically a typical case, the histological picture as shown by the ordinary staining methods is little characteristic. The thionin stain shows up a very small, but distinct, mucin-containing focus which otherwise is hardly noticeable as the connective tissue is almost unaltered.

Twiston Davies' case they were red and vascular and bothered the patient by bleeding. I do not think that either of these patients had the lesions on the ears.

Dr. W. Freudenthal: Sections of one of the small tumours show a fibrous or fibromatous tissue with a marked angiomatous component. At some places the connective tissue is concentrically arranged around the vessels. I think the histology would be consistent with Darier's so-called forme fibroangiomateuse of Pringle's disease. The histological picture is not characteristic enough for me to make the diagnosis on histological grounds only, as I was able to in Bamber's and Twiston Davies' cases. I have not previously heard of lesions on the ears in Pringle's disease, nevertheless, I cannot think of a better classification.

Dr. A. M. H. Gray: So far as treatment is concerned, it might be worth while trying diathermy to one of the lesions and see the effect. As to the name of the condition, I think it would be wise to retain the name "Pringle's disease" as a clinical entity rather than a pathological one.

Dr. A. C. Roxburgh: Diathermy applied to a condition already fibromatous is not likely, I suppose, to make it keloidal?

Dr. A. Burrows: The use of the cautery point is much better than ordinary diathermy, being much more under control.

? **Morphœa with Tuberculous Histology: ? Necrobiosis Lipoidica** (Sections shown by Dr. FREUDENTHAL).—Captain G. LESLIE, R.A.M.C.

This man came along five weeks ago, having been sent by his medical officer on account of patches on the shin which broke down easily and ulcerated. The man is 30 years of age and there is nothing noteworthy in his family medical history. He has served in Egypt and Palestine. The first time he became aware of the condition was in 1941, when he felt two or three nodules on the legs, and applied medicaments to them himself, without any advice from his medical officer. The nodules gradually became red in colour and coalesced to form a plaque in the front of the shin. Fresh nodules developed just beyond the margin and they in turn became reddish in colour and coalesced and joined up with the original plaque. In this way the lesions spread until they reached the stage that members have seen this afternoon. The man also noticed that exercise caused the lesions to be painful, and particularly in hot weather they were irritable.

At present there is a symmetrical, sharply defined patch on the middle of each shin across the tibia. The shape is roughly triangular, being 6 in. by 2½ in. at the base. Its edge is 1 mm. raised above the surrounding normal skin, the central area seems slightly atrophic and is traversed by a number of telangiectases. The colour is a dull red, containing in some places a yellow tinge. The consistency is hard, the surface smooth, but shows a few grooves, apparently the remains of previous small ulcers; hair is absent. On the whole, the appearance is reminiscent of morphœa.

The man has seen various dermatologists and his case was demonstrated as morphœa at two dermatological societies in the North of England. Various tests show nothing abnormal. The blood and urine were normal. The Mantoux test was negative with a high dilution, but on a second test, with a concentrated solution, the result was positive.

W.R. and Kahn tests were negative.

X-ray examination of the chest, abdomen and bones revealed no tubercular focus.

Dr. W. Freudenthal: I excised a small outlying nodule on the left shin of only a few weeks' duration, representing the earliest stage of the condition. It was reddish, round, about 8 mm. across and formed by a firm infiltrate which clinically seemed to involve the upper part of the cutis; the horny layer was thickened.

Histologically, the epidermis is normal apart from some hyperkeratosis and flattening of the rete pegs. The cutis in its full depth, including some tela subcutanea, is transformed into a peculiar granulation tissue. Numerous strands of varying width consisting of fibrocytes, fibroblasts, masses of epithelioid cells and a few giant cells of the Langhans' type surround oval, round, or irregularly-shaped islands of condensed connective tissue, staining pale pink with eosin. A few round foci of densely aggregated lymphocytes are present. The elastic fibres are diminished in the connective tissue islands and are absent within the strands of tuberculoid infiltrate. No lipoids could be found in frozen sections.

It is difficult to make a diagnosis in this unusual case. Combining the clinical with the histological picture, I think this may be an instance of "morphœa with tuberculous histology" of W. N. Goldsmith. Like him, I am inclined to look upon this condition as related to necrobiosis lipoidica (see also Dr. W. N. Goldsmith's remarks on Dr. H. C. Semon's case, *Proc. R. Soc. Med.*, 1944, 37, 648).

POSTSCRIPT (Meeting 15.2.45).—A second biopsy, representing the later stage, was made over the edge of the large, hard plaque on the right shin, including an area showing a yellow tinge.

The term "glossitis" (signifying the presence of actual inflammation) should, I think, not be used, though of course, as I have said, superficial glossitis may occur, as in fissured tongues, especially from retention of food and epithelial debris about the nodules.

The mamilliform nodules, which are not all of exactly the same size, are sometimes surrounded by a deep groove, like the fossa or ditch around a mediæval tower. It has occurred to me that they may in fact represent a dysplastic attempt to produce circumvallate papillæ in the wrong place, just as cutaneous little papilloma-like nodules or pigment spots may represent nipples in the wrong place (vestigial remnants). If this idea of misplaced circumvallate papillæ be correct, microscopical examination might reveal the presence of an aggregation of lymphocytes or a small lymph-follicle below the nodule, and the presence of lymphocytes might be wrongly accepted as evidence of inflammation.

It should be noted that in the first group of mamillated tongues the mamilliform nodules tend to be collected on the lozenge-shaped (rhombic or diamond-shaped) area between the Λ line of circumvallate papillæ and the middle of the dorsum—an area perhaps representing the embryonic median outgrowth ("tuberculum impar"), which, together with the two lateral outgrowths ("tubercula lateralia"), gives rise to the adult tongue (compare especially Martin and Howe, 1938, and Spencer and Cade, 1931). The median line on the distal portion of the dorsum of the tongue apparently represents the site of junction of the two lateral embryonic outgrowths which surround the median outgrowth; and it is about this region that the mamilliform nodules are mainly collected in the second group of mamillated tongues—as in my present case.

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CASE

Mrs. R. B., a somewhat obese Jewish woman, aged 65 years, has recently been in-patient for stabilization of insulin treatment for her diabetes mellitus. She also has high blood-pressure (about 180/110 mm.Hg.) and moderate enlargement of her heart to the



A form of "Mamillated Tongue".

left. Otherwise, apart from the mamillated tongue, which corresponds to my second group, there is nothing special to note. When the tongue condition really developed is uncertain, though it was not noticed before 1942. It has not changed under observation between September 1942 and December 1944. Subjective symptoms, notably a burning sensation, are evidently slight. The photograph was taken in January 1945.

To summarize, mucin is very frequently, though not invariably, found in granuloma annulare. The amount varies. Thionin is the best staining method to demonstrate it.

The President: Has Dr. Freudenthal tried staining any sections in the case just shown by Captain Leslie?

Dr. Freudenthal: Yes, I stained for mucin in Captain Leslie's case, as also in every case of necrobiosis lipoidica, but always with a negative result.

Angiokeratoma.—F. SHERRY-DOTTRIDGE, M.B., Ch.B.

Female, aged 16 years. Two adjacent irregular patches, consisting of raised bluish warty soft nodules, have been present on the right thigh since birth. For the past two years similar small lesions have appeared scattered over both legs. There are no subjective symptoms, and the patient does not suffer from chilblains. There is no family history of similar lesions.

Pathological report on section (Dr. Löwertz): In the upper part of the corium are large oval and irregular shaped lacunar spaces, some of which are divided by thin septa. The spaces are lined with a single row of endothelial cells and are filled with red blood cells, serum or blood-clots. Numerous dilated vessels are seen, some are surrounded by chronic inflammatory infiltration. The horny layer shows hyperkeratosis and in places parakeratosis.

Dr. F. Parkes Weber: I think there can be no doubt that this is microscopically typical angiokeratoma. This condition is a developmental disease in the sense of being *potentially* congenital, though not manifest at birth. Should it be sharply separated from multiple superficial angiomatous or telangiectatic nævus? In certain individuals superficial telangiectases seem to produce (as a result of the extra nutrition, or whatever the cause may be) an excessive growth of the horny layer of the epidermis, in other words, they give rise to angiokeratoma.

The President: Can it be regarded as the same disease as the kind of angiokeratoma which follows chilblain?

Dr. Parkes Weber: I once showed a typical example of the chilblainy type of angiokeratoma, in a physically rather underdeveloped boy, aged 16 years, but there were bony changes in the affected parts (*Proc. Roy. Soc. Med.*, Clinical Section, 1913-14, 7, 25).

Dr. G. B. Dowling: Angiokeratoma was considered to be a disease of the extremities associated with poor circulation. I cannot see that this condition is likely to have anything to do with it. The case looked to me like superficial angiomata. I was also under the impression that angiokeratoma was a disease which tended to come on later rather than very early in life.

Dr. F. Parkes Weber: This type of angiokeratoma is, I think, most commonly seen on the scrotum.

The President: I do not see why the condition should not be called a vascular nævus. I take it that there were no obvious lymph vessels in the section?

Dr. Sherry-Dottridge: No.

A Form of "Mamillated Tongue".—F. PARKES WEBER, M.D.

Cases of mamillated tongue or "*lingua mamillata*" may be divided into groups, especially according to whether the mamilla-like or "papilloma-like" nodules are situated on the proximal half or the distal half of the dorsum. As the nodules are mostly situated near the median line, these two main groups may be termed: (1) *lingua medio-mamillata of the proximal part*, and (2) *lingua medio-mamillata of the distal part*. My present case belongs to the second group, which is the rarer of the two. Most of the first group have been described as examples of "glossite losangique médiane" or "glossitis rhombica mediana" (Brocq and Pautrier, 1914-15, and other references given at the end). The history of the onset of the condition seems mostly to be vague, the patients sometimes having been unaware that there was anything peculiar till their attention was directed by looking at their tongue in a mirror, or by a doctor asking about it. Symptoms, if present, are usually slight and may be partly due to superficial inflammation from retention of food particles in grooves around the nodules. The onset of such slight symptoms may probably attract attention to a condition which has been long present and make both patient and doctor speak of an acute commencement.

I believe that both groups of mamillated tongue are of dysplastic origin and that they are developmental, i.e. *potentially* congenital, though perhaps *not actually present at birth*—in fact, that they are developmental just as the various types of "fissured" tongue are.

The term "glossitis" (signifying the presence of actual inflammation) should, I think, not be used, though of course, as I have said, superficial glossitis may occur, as in fissured tongues, especially from retention of food and epithelial debris about the nodules.

The mamilliform nodules, which are not all of exactly the same size, are sometimes surrounded by a deep groove, like the fossa or ditch around a mediæval tower. It has occurred to me that they may in fact represent a dysplastic attempt to produce circumvallate papillæ in the wrong place, just as cutaneous little papilloma-like nodules or pigment spots may represent nipples in the wrong place (vestigial remnants). If this idea of misplaced circumvallate papillæ be correct, microscopical examination might reveal the presence of an aggregation of lymphocytes or a small lymph-follicle below the nodule, and the presence of lymphocytes might be wrongly accepted as evidence of inflammation.

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Dr. H. S. Stannus: I wonder if examination with a slit lamp would be worth while. It gives a beautiful picture of the tongue papillæ and their structure.

Sarcoidosis.—P. M. DEVILLE, M.R.C.P.

Male, aged 31. He first attended the London Hospital in November 1944 because of a rash on the body and limbs which had appeared about one year previously. He was first taken ill in September 1942 when he noticed dyspnoea on exertion and his chest was X-rayed at a tuberculosis dispensary on two occasions with negative results. In December 1942 he noticed a swelling at the angle of the left jaw; this was diagnosed as parotitis and he had a tooth extracted with no improvement. Later, swellings appeared in the groins. Three months ago dull ache in the left flank especially on exertion. From September 1942 to September 1943 he lost about 2 stones in weight but since then his weight has been steady.

The eruption is mainly on the trunk and arms; a few lesions are present on the face. The lesions are reddish-brown in colour and consist of firm nodules about 3 to 4 mm. in diameter.

The inguinal glands are moderately enlarged on both sides and a few medium-sized glands are present in each axilla. The epitrochlear glands are enlarged and a few small discrete glands are palpable in the cervical region mainly in the posterior triangles.

The spleen is enlarged and palpable about two fingerbreadths below the costal margin. There is no enlargement of the liver.

The cardiovascular, respiratory and nervous systems show no abnormality on clinical examination. He is apyrexial.

* **Investigations.**—Blood-count normal. White cells 8,400. Differential normal. W.R. and Kahn negative. Mantoux 1/100, 1/1,000 and 1/10,000 all negative. Blood sedimentation rate 4 mm. in one hour. Sputum no T.B. found.

Urine strongly acid, light cloud of albumin, a number of leucocytes, a few red cells and granular and cellular casts. Numerous calcium oxalate crystals.

Radiographs.—Chest: Increased hilar shadows. Generalized increase of lung markings and reticular infiltration of both lungs, more marked in the right lung. Hands: A small dense shadow in the middle of the proximal phalanx of the left index finger. Renal tract: A small calculus in the left renal pelvis.

Skin nodule: Section (Dr. Woods) shows miliary nodules of epithelioid cells with no lymphocytes and no caseation. Typical appearance of Boeck's sarcoid.

Dr. Parkes Weber: Skiagrams of the patient's fingers do not show any of the cyst-like appearances in the phalanges, which are typical of certain cases of sarcoidosis. But they do show something else, namely, islands of apparently very sclerosed bone. It would be interesting to ascertain whether similar patches of dense shadowing can be found in other parts of the bony skeleton (e.g. in the pelvic bones). The condition of scattered islands of apparently extremely dense bone, to which I refer, has been called "osteopikilosis" or "osteopathia condensans disseminata" and was first observed in 1915 by Albers-Schönberg.

As for treatment, I wonder whether gold treatment could be tried.

Dr. Deville: We proposed to try some arsenic. In view of his albuminuria, gold treatment might not be without risk.

Dr. Parkes Weber: I understand that one or more American authorities recommend that gold treatment should not be given in any case without the risks being previously explained to the patient.

[February 15, 1945]

Photographic Record of Follicular Keratosis

By H. K. BOURNE

(British Thomson-Houston Company Ltd.)

A PHOTOGRAPHIC method for recording the effect of treatment of follicular keratosis has been devised. The lesions are small and do not differ appreciably in colour from the surrounding area, so that oblique illumination is required to make them easily visible.

A Leica camera with a 1:1.5 extension tube is mounted on an adjustable framework which also carries the lamp for providing the illumination. As the surface of the arm or leg under observation is usually rounded, it is necessary to stop down the camera lens to a small aperture to provide maximum depth of focus. It is also important

to reduce the exposure time to a minimum to prevent the definition from being impaired by involuntary movement of the patient during the exposure, also to use a small concentrated light source to produce sharp shadows. Hence a powerful light source and one of high actinic efficiency was required, and the Mazda 250 watt compact source mercury vapour lamp was chosen. With this lamp, exposures of $\frac{1}{4}$ second at f16 using panchromatic film (23° Scheiner) were adequate with the oblique lighting. The apparatus was also designed to carry a photoflood lamp in a reflector to provide flat illumination, as in some instances flat lighting was quite satisfactory.

With this apparatus the conditions of lighting on the skin are kept constant as the lamp is fixed in relation to the camera and to the skin. A rectangular aperture covering the whole field of view of the camera is attached to it at such a distance that the area enclosed by the aperture is in sharp focus. In using the apparatus it is arranged so that the aperture surrounds and touches the area of skin being photographed.

Vitamin A and the Skin

By HUGH S. STANNUS, M.D., Ph.D., F.R.C.P.

As the result of observations made chiefly among native inhabitants of the Far East a belief grew up that a specific type of dermatosis was due to a vitamin-A deficiency. The dermatosis was of the nature of a follicular hyperkeratosis, and was immediately adopted as a criterion of vitamin-A deficiency. The condition has therefore assumed some importance during the present war.

When in 1942 rapid nutritional surveys in Great Britain, under the aegis of the Ministry of Health, were initiated by Professor Sydenstricker, "follicular keratosis" was one of the signs recorded as indicating a possible vitamin-A deficiency.

These surveys were carried on by Dr. Brunel Hawes and myself and later continued by Drs. Adcock and Fitzgerald.

It soon became apparent that the follicular keratosis we were seeing in this country was very common, especially among children, and further observations showed that it was none other than keratosis pilaris.

Well known to dermatologists and recognized by them as a very common skin affection, it has been "rediscovered", so to speak, by medical men who, interested in nutrition, but untrained in dermatology, may not recognize the condition for what it is.

Already reports are reaching this country from until lately enemy-occupied countries concerning an affection which I believe to be identical with keratosis pilaris but which is not being recognized as such but rather considered as the follicular keratosis associated with possible vitamin-A deficiency. The most recent reference is a letter in the *Lancet* of January (1945) mentioning the condition among East African native troops in Syria.

The condition as seen by us in this country has been recorded while passing in review between eight and nine thousand individuals, of whom more than half were children of school age attending primary and secondary schools.

May I refer briefly to a few points: Among children of the 5-year-old group the condition is seen in its minimal degree and simplest form; as adolescence is approached it becomes more marked and reaches its most exuberant form about puberty and during the next two or three years, a time when the pilosebaceous glands reach their maximum activity and when hormonal influences may be playing a part; especially is this so among girls—and of these, among girls who are particularly well grown and plump.

There appears to be quite a definite seasonal incidence; the lesions become much more marked, fresh areas are involved or the eruption is remarked by the subject for the first time, with the onset of cold weather, and conversely with the coming in of warm weather. There appears to be some evidence too that lack of protective covering—with exposure and trauma in its wide sense, such as friction and pressure—may also play a part. The follicular hyperkeratosis is not uncommonly associated with hyperkeratosis of the skin about the elbows and knees and in some cases, of the skin in front of the ankle-joints, to be distinguished from ichthyosis. Occasionally the follicles on the phalanges may be involved. Grubbiness with lack of or but limited bathing facilities and absence of any kind of skin toilet may also be a contributory factor. In the more marked cases there appears to be a tendency to some increase of pigmentation of the skin in affected areas, more especially around the lesions and also an associated acrocyanosis.

The incidence of keratosis pilaris as noted by us has varied very much in different groups of individuals in different areas. In the 7-14 year age-group among boys the incidence varied from 15 to 55%; among girls 15 to 80%; among male adults 0 to 5%; among female 3.5 to 20%.

Many of our percentages are higher than those given by Pemberton (1940). He found of 3,000 children examined that 5% exhibited "the fully developed condition", and 20% simple enlargement of the hair-follicle, resembling permanent "cutis anserina".

It may be of interest to re-examine the evidence which led to the belief that certain changes in the skin, commonly referred to as "follicular keratosis", were due to a vitamin-A deficiency.

The first description of the condition, one ascribed to vitamin-A deficiency, was given in an article by Frazier and Hu (1931) entitled "The cutaneous lesions associated with a deficiency in vitamin-A in man", but these same lesions were noted many years before, in association with pellagra; by Majocchi (1902) who recognized what he referred to as seborrhœic, keratotic and acneiform follicular pellagrodernis; and by myself in a group of African prisoners subsisting on a grossly deficient diet in 1911, i.e. before the vitamin era. It may also be noted that Seligman mentions seeing keratosis pilaris among the Papuo-Melanesian population of British New Guinea and Torres Straits during the ethnological expeditions of 1894 to 1904. The subjects referred to by Frazier were Chinese soldiers in Peiping whose diet was also a grossly deficient one but whereas in my own cases there were no ocular manifestations, in China the association with keratomalacia led Frazier and Hu to believe the condition was due to a vitamin-A deficiency.

The skin lesions preceded the appearance of the keratomalacia but (to use their own words) "responded to therapy simultaneously with the ocular lesions but more slowly". It should be noted, however, that therapy consisted in the administration of a well-balanced Chinese diet together with one lemon, liver, butter, eggs and 30 c.c. of cod-liver oil daily, so that in no sense was therapy of value as a differential diagnostic test.

The individual lesions and their distribution over the body differed in no way from those described by myself. They will be dealt with below. In 1936 Frazier and Hu published a second article covering a larger number of observations and said "further clinical observations tend to confirm the specific nature (i.e. due to a vitamin-A deficiency) of the hyperkeratosis of hair follicles".

Meantime in 1933—that is two years after Frazier's first article—Loewenthal (1933) published a paper upon "A cutaneous manifestation in the syndrome of vitamin-A deficiency", occurring among prisoners in East Africa. This manifestation he believed to be "new", as far as he was aware, but added that he had no access to the literature. His macro- and micro-scopic findings were similar to those noted by previous observers but of the latter he says: "These histological changes are precisely the same as those of the papule of pityriasis rubra pilaris though of course the two conditions cannot be confused clinically."

Of 1,000 prisoners there were 81 with symptoms which might be referred to vitamin-A deficiency: 71 had night-blindness, 45 xerophthalmia and 75 exhibited the dermatosis. Treatment consisted in giving 1 ounce of cod-liver oil daily. Practically all were cured in rather over two months. To two cases 6 minims of avoleum were administered daily, i.e. a fish liver oil concentrate in cotton seed oil. "The xerophthalmia and night-blindness cleared up promptly, the dermatosis in eight weeks."

Here again the diagnosis of the dermatosis as a vitamin-A deficiency depended upon the association with xerophthalmia and night-blindness and the response to substances containing the vitamin. No explanation is offered of the partial incidence of the affection among the 1,000 prisoners maintained on the same diet. In 1935 the same author reported finding a 30% incidence of this dermatosis among school children and 8.7% among adults of the general native population.

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In a paper the following year Aykroyd says: "Our observations are not incompatible with the theory that vitamin-A deficiency is one of the causative factors of phrynoderma, but the irregularity of its appearance in groups of malnourished children suggests some other factors may play a part." The incidence of the condition among the children housed in 24 hostels each holding 65 boys or 74 girls were 0 to 53% of the boys, and 0 to 46% girls. In 1938 Rao remarked this skin condition among poorer class Indian children attending schools in the Nilgiris. The total number of children, the percentage affected and number treated are not mentioned. The treatment in two cases was as follows: To one boy aged 9, 10,000 i.u. vitamin A, as a concentrate, were administered daily with a good result in four months; the second case, a girl aged 6, responded to 18,000 i.u. daily in nine weeks. The photographs resemble perfectly those of keratosis pilaris, and it should be noted that untreated cases also improved.

The findings in a survey by Fasal (1944) may also here be mentioned. Among 1,482 Malays 2.0% and among 3,656 Indians 25.6% exhibited a follicular dermatosis which exactly resembled the condition found by others. The incidence among children was greater among females than males. Fasal believes the difference in diet is responsible for the racial difference in incidence. He found that red palm-oil with a vitamin-A

(? carotene) equivalent of 1,000 i.u. per c.c. by mouth or applied locally yielded excellent results, while coconut-oil, which contains no vitamin A or carotene, had no effect, but that some cases did not improve unless the intake of protein was increased and vitamin-B complex added to the diet.

The correlation between the dermatosis and those symptoms which are more generally accepted as due to vitamin-A deficiency, is not always demonstrable. Pillat (1929), who was particularly interested in the general signs associated with keratomalacia, described the skin as of a slaty grey or yellow colour, pasty and puffy in earlier cases, wrinkled and lined in later cases, with a dry feeling and a good deal of scurf due to hyperkeratosis, with comedones on the face, but follicular lesions on the limbs and trunk were not mentioned.

The lack of a 100% incidence among individuals of a group under identical conditions has never been explained. Control observations have usually been wanting. The therapeutic tests employed have generally not been exclusive. For many cod-liver oil has been synonymous with vitamin A. The preparations used may have contained other factors than vitamin A, and supplements to the diet have often been made at the same time, or improvement did not occur until supplements to the diet were made.

The nearest approaches to an exact experiment are (1) the two prisoners given 6 minims of "avoleum", a halibut oil concentrate, daily (by Loewenthal), whose dermatosis cleared up in eight weeks, and (2) a case reported by Frazier and Li (1938) which is stated to have responded in great part after fifty-one days' treatment with 2 mg. carotene in olive oil given parenterally. How the carotene was prepared is not mentioned. Aykroyd, perhaps more than any other writer, appreciated some of the possible fallacies attached to the problem.

There is, however, one aspect of the subject which seems to have been overlooked by practically all observers, those mentioned already and others, namely, the possible relationship of the dermatosis under discussion with any of the well-known skin conditions recognized by dermatologists. This may be accounted for I think, as I have already suggested, by two facts: very few of those engaged in work among native races in our colonies and elsewhere had had any dermatological training and, secondly, surrounded by a population living on what appear to be grossly unbalanced diets, the medical man had been inclined to see many illnesses through malnutritional spectacles. No one of the observers cited has ventured upon a differential diagnosis, and it is not without significance that Frazier, writing from Texas in 1943, i.e. eleven years after his original paper, takes the trouble to state that "he never included in his published figures concerning follicular hyperkeratosis the common condition *keratosis pilaris*", but he does not state how he made a differential diagnosis between the two conditions, which I believe to be identical. It might be stated here too that in this last paper Frazier, Hu and Chu report finding only 6.6% of follicular keratosis among 91 children with xerophthalmia of from 2 months to 15 years of age but 45.6% of 103 persons between 16 and 30 years exhibited the condition.

The character of the dermatosis supposedly due to vitamin-A deficiency as described by various observers is as follows: distributed symmetrically the eruption is generally profuse, although in some cases it remains localized. There is often some general dryness and roughness with scaliness and exaggeration of the skin creases giving rise to a wrinkled appearance, associated with hyperkeratosis. In other cases these changes are more or less localized to those areas presenting the typical follicular lesions.

These may appear rather suddenly in some one area and then extend rapidly until the characteristic distribution is attained, involving the anterolateral and posterior aspects of the thigh and the posterolateral surface of the forearm and arm with further extension to the leg and about the elbows, the buttocks, shoulders, axillary folds, the lower part of the abdomen and flanks, and finally the neck and face. The hands and feet are seldom mentioned but in some cases the follicles on the dorsal surface of the fingers may be affected.

At the same time some change in the colour of the skin may also be noted, varying according to race but most marked in the perifollicular region. Among the Chinese the colour is of a yellowish slaty tint, in dark-skinned races a deep brown or black, in white races a dusky purplish brown.

The characteristic lesion is a hyperkeratosis of the pilosebaceous follicles; they present as dry hard pigmented papules, 2 to 5 mm. in diameter, containing a central intra-follicular keratotic plug, many of which project from the hair follicles as horny spines or hard filamentous processes; or the follicle may be covered by a loosely adherent scale, in which case the lesion is conical or hemispherical in shape and may approximate in appearance, especially on the face, the comedo of acne, but pustulation does not occur. The plugs may fall out or be expressed leaving little gaping craters.

A broken hair may often be seen projecting from the centre of the follicle, or on extracting the plug, or removing the scale, a coiled-up hair may be found imprisoned within.

On section—there is found a progressive thickening of the epidermis with acanthosis as the follicle is approached. The follicle in its outer two-thirds is dilated and filled by a plug composed of concentric layers of keratinized material surrounding the broken or distorted hair. The proximal end of the follicle may be degenerated while the sebaceous glands are atrophied or indeed often completely destroyed. In the proximity of the follicle a mild cellular infiltration may be seen; all changes which are probably secondary to the plugging of the follicle.

This clinico-pathological picture of so-called follicular keratosis or phrynoderma one believes to be identical with that met with in *keratosis pilaris*. While a follicular hyperkeratosis is a reaction common to a number of other skin affections, the condition above described may surely be differentiated from all of them.

The first description of the condition, one ascribed to vitamin-A deficiency, was given in an article by Frazier and Hu (1931) entitled "The cutaneous lesions associated with a deficiency in vitamin-A in man", but these same lesions were noted many years before, in association with pellagra; by Majocchi (1902) who recognized what he referred to as seborrhoeic, keratotic and acneiform follicular pellagroderns; and by myself in a group of African prisoners subsisting on a grossly deficient diet in 1911, i.e. before the vitamin era. It may also be noted that Seligman mentions seeing keratosis pilaris among the Papuo-Melanesian population of British New Guinea and Torres Straits during the ethnological expeditions of 1894 to 1904. The subjects referred to by Frazier were Chinese soldiers in Peiping whose diet was also a grossly deficient one but whereas in my own cases there were no ocular manifestations, in China the association with keratomalacia led Frazier and Hu to believe the condition was due to a vitamin-A deficiency.

The skin lesions preceded the appearance of the keratomalacia but (to use their own words) "responded to therapy simultaneously with the ocular lesions but more slowly". It should be noted, however, that therapy consisted in the administration of a well-balanced Chinese diet together with one lemon, liver, butter, eggs and 30 c.c. of cod-liver oil daily, so that in no sense was therapy of value as a differential diagnostic test.

The individual lesions and their distribution over the body differed in no way from those described by myself. They will be dealt with below. In 1936 Frazier and Hu published a second article covering a larger number of observations and said "further clinical observations tend to confirm the specific nature (i.e. due to a vitamin-A deficiency) of the hyperkeratosis of hair follicles".

Meantime in 1933—that is two years after Frazier's first article—Loewenthal (1933) published a paper upon "A cutaneous manifestation in the syndrome of vitamin-A deficiency", occurring among prisoners in East Africa. This manifestation he believed to be "new", as far as he was aware, but added that he had no access to the literature. His macro- and micro-scopic findings were similar to those noted by previous observers but of the latter he says: "These histological changes are precisely the same as those of the papule of pityriasis rubra pilaris though of course the two conditions cannot be confused clinically."

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DISCUSSION

Dr. T. Moore (Cambridge): In tropical countries where they see most of these skin diseases they usually have not got facilities for estimating vitamin A in the blood. On the other hand, in this country, where we have the facilities, we do not get the skin lesions.

Dr. G. B. Dowling: Crandon, an American investigator who gave himself scurvy, noticed a follicular hypertrichosis which had not been there before, and which disappeared when he returned to normal diet. Keratosis pilaris has a definite distribution, as we all know, and the impression I had was that the condition seen in vitamin-A deficiency had not that distribution. We do not see much keratosis pilaris, but the distribution in the deficiency cases seemed to differentiate it.

Dr. W. N. Goldsmith: Like Dr. Dowling, I was struck by the question of distribution. Dr. Stannus described the full distribution as seen by the various workers on vitamin deficiency, and it included what we consider to be the typical distribution of keratosis pilaris, but it seemed to go much beyond it. I should like to know whether, among the cases that Dr. Stannus has seen in this country on adequate diets, many showed involvement of the face and body. In this country I agree with Dr. Stannus that cold appears to play a part. It is a very common associate of erythrocyanosis frigida. There seem to be two kinds of keratosis pilaris, one associated with cold and venous stasis, and the other with xeroderma.

Brigadier R. M. B. MacKenna: On clinical grounds I agree with Dr. Stannus that keratosis pilaris is probably not a manifestation of vitamin-A deficiency. But his paper must be regarded as an interim report, because surely in these cases of keratosis pilaris any degree of vitamin deficiency can be assessed. We have had no statement as to whether the diet of the patients in whom this syndrome was found was truly deficient in vitamin A, and further we have no notion as to whether there might have been some fault of assimilation in their intestinal canals.

Dr. Z. A. Leitner: During the last eighteen months Dr. T. Moore and I have investigated some aspects of vitamin-A metabolism. Five cases of keratosis follicularis (Darier) and two cases of pityriasis rubra pilaris were fully studied and further information was obtained from the examination of about 100 miscellaneous skin cases and the same number of otherwise healthy persons attending for treatment the surgical out-patients' department of St. Mary's Hospital.

The main factors influencing the blood vitamin-A level are: Nutritional intake, interference with absorption (e.g. diarrhoea, steatorrhoea), increased requirements (e.g. thyrotoxicosis, fever, infections, pregnancy, liver diseases), alcohol and vitamin-E intake.

When a definite lack of a single vitamin is shown clinically, one nearly always finds that it is part of a multiple deficiency. This deficiency is mainly dependent on the previously mentioned factors, but the amount of protein, fat and carbohydrate in the diet is also of great importance. This may account for the observation that starving populations—e.g. in continental Europe, where the reduction of vitamin intake is more or less proportional with the reduction of total caloric intake—present much fewer manifestations of certain vitamin deficiencies than could be expected.

As to our results it cannot be denied that vitamin A improved to some extent the skin condition both in Darier's disease and in pityriasis rubra pilaris, provided that it was given in large enough doses for a prolonged time. But this does not imply that these conditions are solely due to an A-avitaminosis nor does it imply that vitamin A can cure these diseases. It is even questionable whether vitamin A itself, or some of its impurities, were responsible for this action. On the other hand, it is evident that despite an appreciable improvement in some cases, in no case could complete healing be achieved in eighteen months although the vitamin-A concentration in the blood had been kept at ceiling level for many months.

Clinically the condition described by Nicholls in Ceylon, so-called "phrynoderma", by Aykroyd in Southern India and by Fasal in Malay is very familiar to Dr. Hawes as seen among Malays, Indians and Southern Chinese and he identifies it with the condition which he and I have been seeing in this country, while the condition as seen in Africa by Loewenthal is also the same as recognized by myself.

Neither of us has seen the disease in Northern China where Frazier made his observations but we believe it to be identical on all the available evidence. Pemberton suggested that the condition in this country "is similar to those described by the older writers under the names lichen pilaris, lichen spinulosus, nutmeg-grater skin and 'scorbutic goosesh' and is an early stage of the condition described by Pillat (1929), Frazier and Hu (1931), Loewenthal (1933) and Nicholls as phrynoderma", and he believed it to be an early sign of a vitamin-A deficiency.

I would state the case the other way round. The conditions observed among Chinese, Indians, Malays, Africans, &c., by these several authors is the same as that known to dermatologists as keratosis pilaris, a condition which was at one time wrongly called lichen pilaris and one which has nothing to do with scurvy. It is not a specific reaction to vitamin-A deficiency. It should also be noted that Pillat did not mention the condition.

This is of course also true of a case under the care of Dr. Helen Mackay in London, published by Goodwin (1934), which was supposed to have responded to vitamin A. All the odd infective conditions, from diaper rashes upwards and downwards, which Dr. Mackay (1934) supposed due to an A deficiency, similarly, I believe, had nothing to do with such a deficiency.

In many of the groups of individuals examined by us in this country there could be no question of an inadequate supply of vitamin A but in some areas this may not have been true.

A more general lack of balance in the diet might well be a factor affecting adversely those congenitally predisposed.

Any disturbance in a native's normal diet is very likely to upset this balance. This is well seen when he is confined in some institution, be it school, asylum or prison. It is well exemplified in imported Tamil labour in Malaya compared with the Malay.

Dr. Hawes disagrees with me I think as to the part played by cold, exposure, &c. It is difficult to disentangle possible factors in causation. Poverty, for instance, entails at the same time poorer food as well as poorer and rougher clothing. The change into the cold season may be accompanied by the disappearance of certain articles of diet. Many native races are both poor, ill-fed, ill-clothed, unwashed and exposed. Even in Singapore, with a temperature range of 90° to 70°, a sudden drop to 70° produces the same effect as say a drop from 55° to 40° in this country.

This brings me to another point. Berès, in a Paris thesis (1928), refers to two adult cases of keratosis pilaris, one under the care of Jeanselme, the other of Besnier, in which the eruption appeared suddenly, in the one after a fall from a horse, in the second case the exciting cause was exposure to cold, and suggests that the lesions remained latent and unnoticed until excitation of the sympathetic caused them to become apparent.

This theory of sympathetic excitation acting upon the erectors pilorum is not without interest in view of the effect of cold—and possibly of fear. As far as I know there is no reference to these muscles in keratosis pilaris, but Nicolau (1918) described them as hypertrophied in the follicular lesions of scurvy met with in Serbian soldiers during the last war, an outbreak which was also the subject of an article by Wiltshire (1919).

The experimental production of skin changes comparable to those of supposed vitamin deficiency or of keratosis pilaris has been rather neglected. Moul't's work on the rat (1943) is, however, the most interesting. He submitted a series of groups of animals to a series of diets, each containing less and less vitamin A, from 50 to 0 i.u. so that the progressive changes in the skin resulting from the degree of deficiency and the period of deficiency could be studied histologically. The resulting pathological picture, including all the typical changes in the pilosebaceous follicle, closely resembles that seen in keratosis pilaris. The form in which the vitamin was administered is not mentioned but Dr. Moul't has kindly informed me it was a fish liver oil concentrate of high potency diluted with edible ground-nut oil.

The matter is further complicated by the fact that for the absorption from the bowel and storage in the liver of vitamin A other substances must be present, chief among these perhaps is tocopherol or vitamin E. These act as "anti-oxidants" or "protectors" substances. It would be possible therefore to postulate a "conditioned" vitamin-A deficiency.

Again in turn the absorption and utilization of unsaturated fatty acids is bound up with an adequate supply of pyridoxin or vitamin B₆, both concerned with the nutrition of the skin.

CONCLUSIONS

(1) The condition called follicular keratosis, phrynoderma, &c., appears to be identical with keratosis pilaris.

(2) The actual pathogeny of the condition remains uncertain.

(3) It seems questionable whether a vitamin-A deficiency should be looked upon as a specific cause, though under certain circumstances it may be a factor in causation.

(4) I would suggest that keratosis pilaris, as seen among all races, is a reaction in a predisposed skin—to a disturbance in its normal metabolism. The disturbance may be in part traumatic, due to cold, &c. and/or in part nutritional, due to a relative lack of some one or more essential food factors including vitamin A, vitamin E, vitamin B and fatty acids, associated with dietetic deficiency or deficient absorption.

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The main factors influencing the blood vitamin-A level are: Nutritional intake, interference with absorption (e.g. diarrhoea, steatorrhoea), increased requirements (e.g. thyrotoxicosis, fever, infections, pregnancy, liver diseases), alcohol and vitamin-E intake.

When a definite lack of a single vitamin is shown clinically, one nearly always finds that it is part of a multiple deficiency. This deficiency is mainly dependent on the previously mentioned factors, but the amount of protein, fat and carbohydrate in the diet is also of great importance. This may account for the observation that starving populations—e.g. in continental Europe, where the reduction of vitamin intake is more or less proportional with the reduction of total caloric intake—present much fewer manifestations of certain vitamin deficiencies than could be expected.

As to our results it cannot be denied that vitamin A improved to some extent the skin condition both in Darier's disease and in pityriasis rubra pilaris, provided that it was given in large enough doses for a prolonged time. But this does not imply that these conditions are solely due to an A-avitaminosis nor does it imply that vitamin A can cure these diseases. It is even questionable whether vitamin A itself, or some of its impurities, were responsible for this action. On the other hand, it is evident that despite an appreciable improvement in some cases, in no case could complete healing be achieved in eighteen months although the vitamin-A concentration in the blood had been kept at ceiling level for many months.

It is certain that the initial claims as to the healing effect of vitamin A in dermatology were exaggerated. To reduce these claims to reasonable level was the aim of our prolonged experimental work and it is hoped that the results with the exact data will be presented at an early date.

Dr. H. Pollak: A rash of what looks like follicular hyperkeratosis is not uncommon in patients with carcinoma of the stomach. Here, according to Rhoads and his associates, the blood vitamin-A levels tend to be low, but cannot be raised by even large amounts of vitamin A. However, brewer's yeast brought about a significant rise in blood vitamin-A levels. There is, in general, much to suggest an interaction in metabolism between vitamin-A and vitamin-B complex, and it is difficult to say which vitamin is ultimately concerned. Even with regard to the photochemistry of visual purple, it is not certain whether B vitamins, perhaps riboflavin, are required for the utilization of vitamin A, or whether there is a relationship the other way round.

Dr. S. R. Brunauer: Shortly after S. Peck in the United States had published his paper on vitamin A and Darier's disease (Peck, S. M., Chargin L., and Sobotka, H. (1941), *Arch. Derm. Syph.*, Chicago, 43, 839), investigations were started at St. John's Hospital on the influence of vitamin A upon Darier's disease and other skin conditions, the results of which A. D. Porter and E. W. Godding are about to publish. In Darier's disease hardly any benefit was observed even after large doses of vitamin A had been administered. In cases of lichen pilaris there was no improvement either and the same applies to other skin conditions, e.g. ichthyosis, dry eczema. On the other hand, one case of pityriasis rubra pilaris cleared up with vitamin A as reported by A. D. Porter and E. W. Godding (*in press*). Whether this was a coincidence is difficult to say; at any rate the comments Dr. Leitner has made to-day suggest that the improvement was not purely incidental.

Mr. A. L. Bacharach: A low fat diet might seriously interfere with the absorption of carotene. We know nothing of the mechanism for conversion of carotene into vitamin A, and that introduces a further complication.

Dr. R. Brunel Hawes: Our observations on children suggest that vitamin-A deficiency has no relation to the skin condition. In the East I have given vitamin A by injection in large doses without observing the slightest effect on the skin. In this country we have taken batches of children showing various degrees of keratosis pilaris and given different batches vitamin A, vitamin C, and nicotinic amide without observing any alteration. I feel that the condition is possibly due to a relative deficiency of some fat or fatty acid to the carbohydrate intake. If this is so, one would therefore expect to see it more often in the East where the fat intake may drop to 8 to 11 grammes a day, and an increase in wartime in this country, especially in children of the "eating age", i.e. the second decade of life, when the carbohydrate intake would increase but the fat intake being rationed would remain the same.

The President: It does seem a little difficult to accept Dr. Stannus's theory entirely, because keratosis pilaris is always described as a congenital and familial condition, appearing about the age of 2 or 3, and persisting indefinitely. It affects the extensor aspect of the limbs, and rarely the face. This alleged vitamin-A trouble, as most of the accounts agree, occurs suddenly in people of varying ages. I agree that it is very commonly on the extensor aspect of the limbs—the front and sides of the thighs and the back and sides of the forearms. Keratosis pilaris is usually most marked on the back of the upper arms. The hyperkeratosis of scurvy is mainly on the buttocks and backs of the thighs and calves. I think there is something to be considered about the distribution.

Dr. Stannus (in reply): With regard to the distribution in keratosis pilaris, I would suggest the lesions are more widespread than some accounts of the disease would lead one to believe. This is an opinion based on the examination and study of hundreds of cases. Only by seeing large numbers in a comparatively short time is it possible to recognize the many variations in the evolution and distribution of lesions in this affection. In these and other respects I believe so-called "phrynoderma" is identical with keratosis pilaris.

The President has said that he thought "phrynoderma" was sudden in onset. Only one author has alluded to this. The same has been noted in keratosis pilaris and it always has to be remembered that suddenness of onset may only mean suddenness of recognition. Beres thought the lesions might be latent and then obvious as a result of sympathetic stimulation.

The biochemical aspects of the possible relationship of vitamin A and carotene with the skin are a most interesting study.

Pityriasis Lichenoides et Varioliformis Acuta.—G. B. DOWLING, M.D.

Male, aged 34. First seen on December 29, 1944, when he complained of a profuse eruption characteristic of pityriasis lichenoides et varioliformis acuta. There was a history of acute onset a month before. A month later the eruption was seen to be clearing up fairly rapidly. The case is shown as an example of this condition clearing up spontaneously within a comparatively short time.

The President: It is very interesting to see a case which has cleared up spontaneously.

Pemphigus Vegetans.—LOUIS FORMAN, M.D.

Miss I. M., aged 25.

October 1944 complained of soreness of mouth and oozing areas on the scalp. Seen December 1944 with vegetating plaques groins and scalp. There were also discrete, raised areas showing vesico-pustules at edges. There were superficial ramifying mucous patches on the gums and adjoining mucous membranes.

27.11.44: W.B.C. 16,000, eosinophils 21%. Cultures from the vegetating lesions on scalp gave hæmolytic streptococci, staphylococci and diphtheroids.

7.12.44: Sulphamezathine 36 grammes given over period of five days. Very considerable improvement in general condition and the vegetating lesions on the scalp and in the groins disappeared. The mouth, however, still remained affected.

15.12.44: Scalp condition recurred. 50,000 units penicillin sprayed on scalp over period three days without definite benefit.

28.12.44: Sulphathiazole 36 grammes over five days. Improvement but rapid relapse.

5.1.45: 600,000 units penicillin given intramuscularly over six days with slight improvement only. Vegetating lesions on scalp have recently relapsed. There are ring-shaped blisters and mucous patches on the lower lip and gums are covered with grey, superficial, necrotic epithelium, forming a ramifying pattern.

The President: I have had a number of cases treated with suramin or antrypol, and the improvement was astonishing. I do not say the cases were of real pemphigus. They may have been only dermatitis herpetiformis, but they cleared up in a remarkable way, and two cases of pemphigus foliaceus have done the same. I think antrypol is less toxic than the original germanin.

Necrobiosis Lipoidica, ? Schamberg's Disease.—THERESA KINDLER, M.D., for R. T. BRAIN, M.D.

Male, aged 61, printer. Healthy-looking man. No relevant family history. For ten years slow increase of yellow spots and patches on both shins, without any subjective symptoms. Two years ago he developed hidradenitis in both axillæ. His doctor found sugar in his urine and referred him to hospital.

The front of both legs and feet is largely covered by a lemon-yellow discoloration. It is diffuse in the centre, at the borders merging into spots the size of a pin-head or a lentil. A marbling of telangiectases, minute hæmorrhages, dilated venules produce a mottled appearance. On glass pressure there remains a yellow infiltrate. The epidermis is smooth, thinned, shiny. Scattered over the ankles are tiny red and larger yellow spots. There is a shallow, farthing-sized, depressed, circular scar from an ulcer on the right shin. The rest of the skin and mucosa normal.

B.P. 270/100, pulse regular, artery thickened, tension high. Total blood cholesterol 200 mg.%. Urine: Traces of sugar. Fasting blood-sugar 132 mg.%, after carbohydrate meal 207 mg.%. Patient is controlled on reduced carbohydrate diet, without insulin.

Biopsy (Dr. Loewenberg): In the middle and lower layers of the cutis the collagenous tissue appears in multiple areas as a structureless mass, poor in nuclei, with homogenized, unevenly staining bundles. In Van Gieson's stains the brilliant red collagen bundles are intermingled with yellow ones. The elastic fibres, though well preserved in the upper layers, are partly missing in the more damaged areas, those present are coarse, broken, clumped together. There is a scanty infiltrate round some of the necrotic areas, but more infiltrate in the upper part of the corium, consisting chiefly of lymphocytes and connective tissue cells. Striking vascular changes in all layers; the adventitia thickened, with its layers concentrically arranged, the intima cells swollen, the lumen narrowed, sometimes obliterated. There is bleeding into the tissue and blood pigment is present. With Sudan III some of the necrotic areas are stained a faint yellow; there are scanty red globules between the bundles.

The papillæ and rete pegs are missing, the epidermis atrophic. The epidermis-cutis border runs in a straight line.

The clinical appearance with the symmetrical distribution, extensiveness of the lesions, the red cayenne-pepper-like spots at the ankles would suggest Schamberg's disease, though the ulceration and the definitely lemon-yellow infiltrate are not features of this condition. On the other hand the histological picture, with the necrosis of the collagenous and the damage to the elastic tissue, the vascular changes which are more on the proliferative side than showing dilatation and new formation of vessels, the scanty infiltrate may be pointing towards necrobiosis.

Dr. W. Freudenthal: In my view the diagnosis of Schamberg's disease would be consistent with the clinical and histological aspects of the case.

Leprosy, Mixed Form.—E. W. PROSSER THOMAS, M.D.

Greek seaman, aged 29, unmarried; from the Calamata district. Has been in England periodically for six years. Ten years ago he noticed loss of feeling over the knees, especially the right, then over the thighs, ankles and arms. He has burned himself in various places from time to time. Three years ago he was in hospital at Alexandria with fever of unknown origin. Two years ago a patch of thickening appeared on the inner side of the right ankle. During the past few months nodules have been developing on the face, arms, thighs, and legs. He says his general health is good. No history of coryza or epistaxis.

On examination, the general texture of the skin appears soft and not especially discoloured. Firm nodules of varying size, hemispherical, dull pink, rather shiny, are present on the face, arms, thighs, and legs. Large patch of brown pigmented erythema inner aspect right arm, due (he says) to a burn. Scars over points of elbows and elsewhere, apparently from trauma and burns. Patchy anaesthesia right forearm (flexor surface), and across right ankle, also on thighs. All superficial lymph nodes enlarged. Both ulnar nerves thickened. No organisms found in nasal smears. W.R. negative.

Dr. Stannus has remarked on the diffuse thickening of the forehead above the superciliary arches and of the *peau d'orange* appearance of the skin in these areas, which he considers characteristic.

Brigadier R. M. B. MacKenna: I have seen a moderate number of cases and I gather that the experts in leprosy think that the nasal smear is a very inexact method of testing. I understand that in many cases microscopic examination of a strip taken from the perineural sheath of the ulnar nerve—if that nerve is thickened—is often a more reliable test.

Dr. H. S. Stannus: If the light is thrown on this patient's forehead it will be seen that there is a very mild diffuse infiltration in the supra-orbital region, and I believe I could make a clinical diagnosis on that alone. It has not got to the stage of furrowing.

Dr. Brunel Hawes: In searching for leprosy bacilli I agree that nasal smears are very unreliable. A skin clip taken from the lobe of the ear and the under surface rubbed on a slide will often show bacilli when other tests are negative even though the skin of the ear appears normal. Sometimes a leper may be exuding so many bacilli that a slide pressed on the skin and then stained will show them, and in other cases they cannot be found even after a long search. One negative result is not of much value. I observed one man with nerve leprosy from the start of his illness to his death from carcinoma fifteen years later, and post mortem could not find any bacilli in any of the nodular enlargements of the nerves in his body.

POSTSCRIPT.—The diagnosis was confirmed by biopsy.

Section of Radiology

President—J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

[October 20, 1944]

Bone Tumours and Their Radiological Implications. [*Abstract*]

PRESIDENT'S ADDRESS

By J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

THE speaker called attention to the difficulties in radiological interpretation and the misunderstandings which were liable to occur if too much stress were laid on radiographic features without reference to the clinical findings and other means of investigations at the disposal of the radiologist. He considered that it was unscientific to state dogmatically that radiographic features alone were sufficient to establish the nature of any bone tumour or to place complete reliance on bone changes which hitherto had been considered as typical of a specific lesion. He illustrated these points by showing a series of radiographs of bone tumours collected over a period of twenty years. His examples included a series of bone lesions all of which showed periosteal reaction producing the "sunray effect" which was once considered to be diagnostic of osteogenic sarcoma, but which in each case shown represented a different pathological condition (figs. 1, 2, 3). He pointed out that similarly osteolytic lesions, although producing similar radiographic features, could also represent entirely different pathological conditions (figs. 4, 5, 6, 7). Further radiographs showed the confusion which often resulted from the lack of co-operation with the Pathological Department and from the scanty information often given to the pathologist (fig. 8).

Dr. Grout concluded his Address by pointing out that the series of radiographs shown were meant to illustrate the need for a more careful follow-up of cases and a better system of co-operation between the surgeon, pathologist and radiologist. He deplored the present system which did not permit of time or place for discussion on difficult cases. He was aware that a committee, for the purpose of collecting cases of tumours of bone, formed by the Association of Orthopædic Surgeons, existed before the war but he hoped that when activities were resumed it would enlarge its scope and include all those interested in the problems of disease of bone. A department of radiology in any hospital was in a unique position in so much that patients from all other departments were referred there for examination. He felt, therefore, that the department of radiology should share the responsibility of proper recording and the efficient follow-up of cases.

[Meeting of November 17, 1944, appeared in the issue of February 1945, page 147, vol. 38. Meeting of January 19, 1945, will appear in a later issue]

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FIG. 4.—Osteogenic sarcoma (osteolytic type).

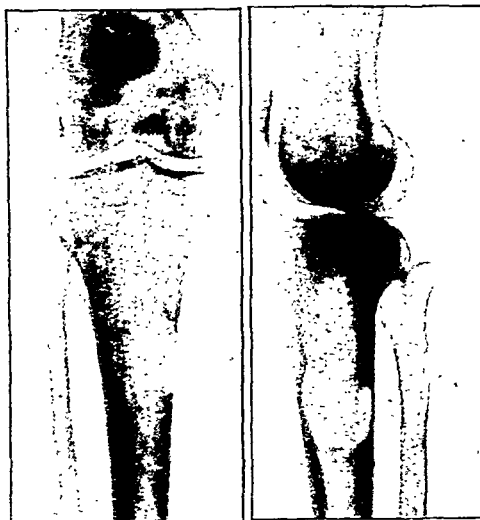


FIG. 5.—Secondary to malignant tumour of the kidney.



FIG. 6.—Plasmocytoma.

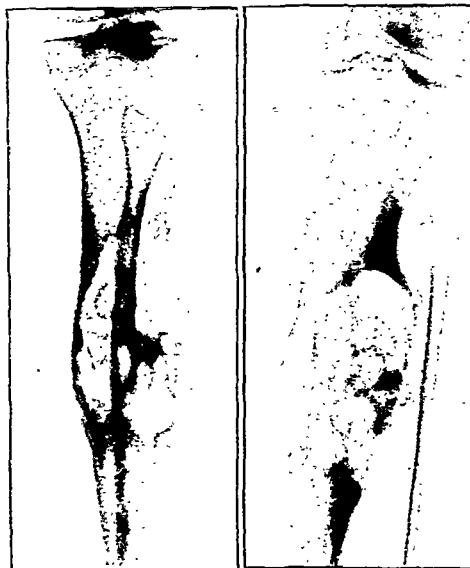


FIG. 7.—Localized fibrocystic lesion.

FIGS. 4, 5, 6 and 7.—Examples of bone destruction presenting similar radiographic appearances with different pathological conditions.



FIG. 1.—Osteogenic sarcoma.

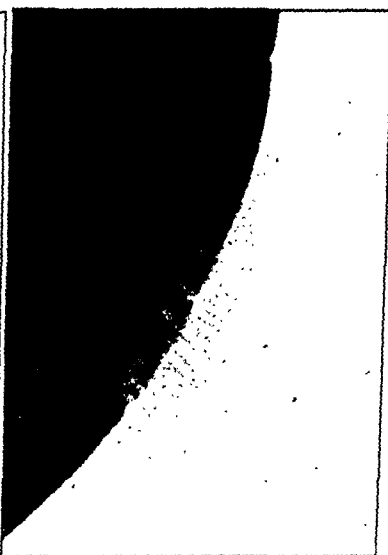


FIG. 2.—Neuroblastoma.

FIGS. 1, 2 and 3.—Examples of three different lesions each showing the "sun-ray effect".

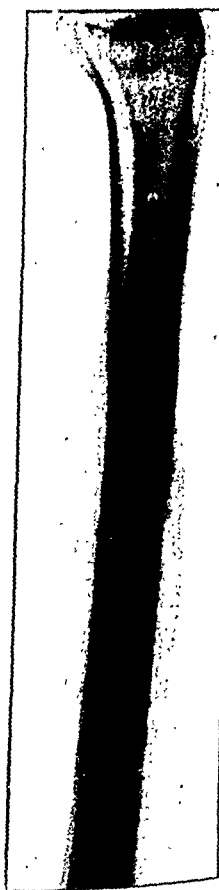


FIG. 3.—Metastases from cancer of the breast.



FIG. 8.—Malignant tumour of the pelvis showing extensive bone destruction. Examination of specimen obtained by aspiration biopsy showed no malignant changes. The misleading pathological finding was probably due to faulty technique in obtaining the specimen.

FIG. 8.

The X-ray counterpart of this type of treatment, subcutaneous X-ray therapy, has been developed by Mr. Lambert and Dr. Watson in Manchester, and was described by Mr. Lambert at a Meeting of the Section of Laryngology of this Society in December 1942.

TABLE IV.—INTRINSIC CARCINOMA OF THE LARYNX.
Subcutaneous X-ray Therapy.

Two-year survival ...	64% of 29 cases
One-year survival ...	65% of 17 cases

In this whole group of patients I could find but one suitable for the Finzi-Harmer technique.

The Finzi-Harmer technique, as the most localized of all in its effects, should be used only for a small tumour isolated on a mobile cord, and toward the middle of it. So used it is, naturally, the most successful technique. Results are shown in the next table:

TABLE V.—CARCINOMA OF THE LARYNX.
Finzi-Harmer Technique.

Three-year survival ...	85% of 28 cases
Five-year survival ...	71% of 15 cases

Many of these cases were treated years ago, before the limitations of the method were appreciated; even better results could reasonably be expected from better selected cases.

This completes a review of carcinoma of the larynx regarded as a progress from great to small; first the 60% with added secondary disease who, for practical purposes, may almost be written off as far as cure is concerned, and then the 40% of potentially curable cases, in whom tumour size is presented as the most important single factor, not only in prognosis, but in the design of a suitable treatment.

Dr. S. Bryan Adams. Further investigation is required into the time-dose factor when treating neoplasms of the larynx.

That a period of a month or more is not essential for the adequate radiotherapy of a squamous carcinoma occurring in other locations is well known. In certain sites it is possible to remove an epithelioma with a single dose of radiation. Although present work shows that the destructive power of irradiation may be greater when spread over a longer period the destruction of normal tissues may also prove to be greater, if only because of their relatively slower rate of growth.

Fenestration is a method used for an intrinsic carcinoma of the larynx which makes use of a much shorter time period. Some of the failures following this technique may be due to the radium containers being badly placed, e.g. unless the window is carefully cut the cord may be at the level of the blind ends of the containers.

Another method using a short time period is the skin-reflection method. We have treated a small number of cases by this method and no claim is made other than that the initial results are encouraging and seem to justify further investigation. The technique is simple. The skin is reflected under local anaesthesia and a reasonably large dose of X-radiation is given through one or two portals, in most cases centred directly on the lesion. Following the initial treatment the method is capable of considerable modification. The need for such will be considered at a later date when it is easier to judge results.

The advantages of this method are: The initial modification of the tumour is complete in the small series treated. The absence of skin reaction adds greatly to the patient's comfort. Glandular metastases have been locally excised when making the skin flap and should these develop at a later date either surgery or further radiation may be considered. An elaborate set-up which has constantly to be repeated is avoided.

The cases treated include chiefly tumours of the pyriform fossa, although the growths of the vallecula and of the vocal cord have also been dealt with. Nine cases only have been treated. Two of these are dead or dying, owing to spread into the base of the tongue and metastatic formation. The others are well and the primary has completely healed up to present date. The longest survival so far without recurrence is just over two years although most of the cases have been treated comparatively recently.

My surgical colleagues have been sufficiently impressed by the method to encourage its further development and I am particularly indebted to Mr. A. J. Wright for the constant help and encouragement he has given in the conduct of these cases and to Mr. R. G. Boyd for his help in performing satisfactory skin reflections.

These results therefore show that it is possible to cause the disappearance of laryngeal growths for a considerable time by the short period method of irradiation and further investigation is indicated.

[February 16, 1945]

DISCUSSION ON RATIONALE OF RADIOTHERAPEUTIC TECHNIQUE IN CARCINOMA OF THE LARYNX. [Abridged]

Dr. J. L. Dobbie (*Holt Radium Institute, Manchester*): The general object of this discussion of carcinoma of the larynx is to show how a range of techniques is called for, suited to various stages of disease.

Table I illustrates the percentage occurrence of different types and stages as found in a large series of cases:

TABLE I.—PERCENTAGE GROUPING OF 282 CONSECUTIVE CASES OF CARCINOMA OF THE LARYNX.

No nodes	Intrinsic	Extrinsic	Total
Nodes present	19	21	40
		5	55	60
		24	76	100

I am using "intrinsic" to imply that the disease is confined within the larynx and does not pass upward beyond the aryepiglottic folds. Under "extrinsic" are placed all growths arising in the laryngopharyngeal region which involve any of the laryngeal structures, including vallecula, epiglottis, and pyriform sinus, but excluding post-cricoid cancers.

Analysis of a larger group of treated cases shows that while 29% of the "no nodes" group survived five years, only 4% of those having nodes did so. Because of the dominating influence of secondary disease, patients presenting themselves with this already present will not be further considered in this discussion.

In practice a continuous sequence from large extrinsic to small intrinsic lesions is found. The larger pharyngo-laryngeal tumours can only be treated by external radiation, and frequently extend to the very limits of small-field, beam-directed X-ray therapy—a type of treatment that begins to show its characteristic advantages only when fields of 6 cm. diameter or smaller can be used.

As fully developed, the method has been in use for five to six years and groups available for long-term analysis are still small. In order to present five-year survival rates I have been forced to go back to times before satisfactory beam-direction, or, perhaps, any at all.

TABLE II.—X-RAY TREATMENT OF CARCINOMA OF THE LARYNX—1932-39.
5-year Survival Rates.

Intrinsic	18% of 18 cases
Extrinsic	9% of 22 cases

These numbers are small and really reflect the preponderance of radium treatments in earlier years, and you may be sure the worst was left for the X-ray tube. In fact, in this series three cases in both intrinsic and extrinsic groups were treated by radium for one by X-rays.

For interest, I have collected the three-year survival rates of more recent treatments in the same category, that is to say, cases of substantial tumours calling for relatively large-volume treatment. These are only three-year figures, but perhaps they suffice to give an idea of an improved expectation of survival:

TABLE III.—SMALL FIELD X-RAY—1930-41.
3-year Survival Rates.

Intrinsic	42% of 25 cases
Extrinsic	25% of 20 cases

We have not used this technique for smaller fields than 6 by 4 cm., feeling that a tumour that can be so covered could often enough be better handled by techniques resulting in less volume dosage than several beams of even this small cross-section.

These other techniques involve operative exposure, and therefore should probably be restricted to intrinsic cases, of which there is a considerable group much beyond the scope of the Finzi-Harmer fenestration technique.

In this group the method of implant after complete removal of the cartilage (Morton, Gray and Neary, *Brit. J. Radiol.*, 1944, 17, 204-212) should be suitable.

Average doses to the centre of the tumour are 5,000 r gamma radiation plus 800 r to 1,000 r X-radiation. The treatments are given concurrently and the overall treatment time is four to five weeks.

Results.—Of 29 patients treated in various stages of the disease (intrinsic and extrinsic, with and without glandular metastases) 7 are alive at the end of three years, 1 died of intercurrent disease and 1 is untraced. 19 died of malignancy and in 1 patient the cause of death is unknown but he was not symptom-free after treatment and may be assumed dead of malignancy. Taking 20 dead of malignancy and 7 alive, the survival-rate is thus 26% for all stages.

Many of those dying of malignancy had direct extension of the growth upwards or downwards. It must be remembered that the diameter of the radium beam is small, and for treatment to be successful the vertical limits of the growth must be very circumscribed.

Dr. Benjamin Jolles: The fact that neoplastic tissues in the larynx, *ceteris paribus*, respond differently to radiation in the absence or presence of œdema in or around the growth, renders the early detection of this complication very important. Soft tissue radiography which is complementary to laryngoscopy is of great value if undertaken in a methodical way. Apart from a plain lateral radiograph and a tomographic film, a picture taken with a barium swallow may throw additional light as regards the surface of the growth to which the opaque particles stick; generally it does not happen over an œdematous area. A fourth film with the Valsalva manoeuvre reveals the degree of limitation of movement of the cartilaginous framework in the air-expanded larynx-pharynx, and gives a clue as to the extent of the invasion by growth and details regarding œdema. This picture shows also the effectiveness of the treatment and after its completion may foretell sequelæ and recurrence.

In the intensive type of treatment the problem of connective tissue reactions is of paramount importance and therefore the detection of a slight degree of œdema of the recurring-substiding type may influence the way of approach. A qualitative physiological approach in such cases is imperative and Coutard's views on the more rapid delivery of the dose if the œdema follows, or a slower rate of irradiation if œdema precedes the gradual involution of the irradiated tumour, are worth remembering.

As no single measure can be effective in combating or preventing œdema due to manifold causative factors, general lines based on the knowledge of the physiopathology and radiobiology of the underlying changes in the tissues must be adopted. Among substances which seem useful during the radiation treatment for carcinoma of the larynx, sprays of urethane and cocaine have proved helpful in this respect in 8 of my cases.

As regards the modification of the Finzi-Harmer technique R. Kaye Scott of Melbourne has been working on similar lines (*Aust. med. J.*, 1932 (ii), 287).

Dr. N. S. Finzi said that he had had bad results in extrinsic laryngeal growths even with the million volt machine. With regard to intrinsic growths the patient's life must be the prime consideration, but if the case were suitable there was no question as to which gave the better results, radiation or surgery. He then played some gramophone records of the voice in laryngofissure cases and in radium implantation cases. These showed the almost normal voice obtained after the radium method as compared with even the good laryngofissure voices.

Dr. H. C. Simchowitz mentioned a new method of intralaryngeal contact therapy of carcinoma of the larynx, recently described by Chaoul, who has used this method in suitable cases since 1940. Chaoul had constructed for this purpose a modified contact therapy tube fixed to a specially constructed direct laryngoscope and reported 11 three year cures, with a good functional result, out of 13 treated cases.

The speaker would like to know whether radiotherapists had experience with the "concentration method" of radiotherapy for carcinoma of the larynx—the use of large daily doses over a comparatively short period—described recently by Cutler, who claimed its effectiveness in the more radio-resistant types of carcinoma.

Dr. Frank Ellis: The principles to be observed in treating carcinoma of the larynx by radiation would appear to be: (a) Economy of radiation; (b) accuracy of application; (c) evidence of the best time-dosage relationship; (d) avoidance of the ill-effects of sepsis.

Economy of radiation.—As little radiation as possible should be absorbed in normal tissues for a certain tumour dose. The most economical methods are undoubtedly the

Case	Date treated	Type	Present state
42/1376	20.1.43	Pyrimiform fossa	Well
43/10	2.2.43	Vallecula	Dead
44/87	7.2.44	Vocal cord	Well
44/280	28.2.44	Pyrimiform f. Epiglottis	Dying
44/411	1.5.44	Pyrimiform f. Epiglottis	Well
44/1546	29.10.44	Pyrimiform f. Epiglottis. Arytenoid	Well
44/1615	1.11.44	Vocal cord. Arytenoid. Gland. metas.	Well
44/1748	6.11.44	Vocal cord. Ant. commissure. Epiglottis	Well
44/1803	20.11.44	Pyrimiform fossa	Well

Dr. M. Lederman [*Abridged*]: At the Royal Cancer Hospital intrinsic cancer of the larynx is treated exclusively by telerradium therapy. The techniques used are based upon the following considerations:

(1) *Apparatus and physical conditions of treatment.*—(a) A 5 and a 1 gramme telerradium unit are used, the former being of the Radium Beam Research pattern. Fields varying in size from 3.5 cm. to 8 cm. diameter circle are available, and accurate small field techniques are possible. Green's directional caliper is employed for both beam direction and dose measurement. (b) Very short wavelength, highly penetrating radiation is used at short focal skin distances: 5 to 8 cm.; because of this the beam of radiation is diffuse and the percentage depth low—two distinguishing features of telerradium treatment that technically have to be fully utilized.

(2) *Biological considerations.*—A protracted, fractionated scheme of dosage is adopted. The dosage rate varies from 5 to 8 r/min. at the surface. Two treatments of 220 to 340 r surface dose per day are given for six days per week and the total treatment time is four to six weeks. The tumour dose varies considerably from case to case, the range being 5,000 to 10,000 r with 7,000 r as an average. The integral dose is low, usually 1 to 2-megagramme röntgens.

(3) *Clinical considerations.*—Treatment is individualized according to the needs of each patient, no attempt being made at any routine standardization of technique. In each case the initial treatment plan is based upon: (i) The general condition of the patient and the presence or absence of complications, such as infection, cartilage invasion, or respiratory embarrassment. (ii) The site, extent and possible mode of spread of the disease. In this connexion a study of the behaviour and mode of spread of intrinsic cancer of the larynx shows that it is possible to divide the cases encountered into four topographical types, namely, those where the anterior half, the posterior half, one side, or the centre of the larynx are involved by the disease. The accurate assessment of the topography of the tumour is of prime importance in deciding upon the appropriate treatment technique.

The conduct of the treatment depends on the response of the patient, the tumour, and the normal tissues subjected to irradiation. Our main object is to obtain a heterogeneous field of radiation with maximal dosage at the tumour site, as little radiation as possible being given to the normal laryngeal and adjacent pharyngeal tissues. No attempt is made to obtain uniform dosage throughout the larynx, nor is a fixed prescribed dose of radiation employed. Clinical judgment and not any hypothetical concept of cancericidal dose is the guide to the total tumour dose given.

Slides were shown illustrating the technique of treatment of intrinsic cancer affecting the following parts of the larynx: (1) Cord tumours: (a) Anterior half of the larynx; (b) posterior half of the larynx; (c) unilateral larynx; (d) the central part of the larynx. (2) Supraglottic tumours. (3) Subglottic tumours. (4) Lymph-node metastases. (5) Post-laryngectomy cases.

Dr. Phyllis Wade: I propose to describe in brief a series of cases of carcinoma of the larynx treated at the Leeds Radium Centre by a technique employed by Lieutenant-Commander La Touche.

From observations of radiation reactions it is apparent that the laryngeal cartilages and other normal structures adjacent to a laryngeal carcinoma are more tolerant to high dosage irradiation by gamma rays than by X-rays. In many cases gamma radiation is most suitably administered by means of the radium beam, but lateral protection of the bomb head often obstructs the setting of lateral fields far back. Furthermore, the low percentage depth dose tends to nullify the value of a central posterior field. Thus it may follow that treatment by radium beam alone raises the anterior portions of the growth to a higher dose than the posterior part which is consequently under-irradiated. The dose to the posterior part of the larynx is, therefore, raised by the addition of an X-ray field in a central posterior position.

Section of Laryngology

President—C. GILL-CAREY, F.R.C.S.ED.

[February 2, 1945]

DISCUSSION ON TREATMENT OF CARCINOMA OF THE LARYNX

E. D. D. Davis: *A review of 40 cases of laryngofissure for early intrinsic carcinoma of the larynx.*—This review has been undertaken to ascertain: (1) the features of those cases which are suitable for a successful laryngofissure; (2) the value of some modifications and details of the technique of the operation; (3) the results of the operation particularly in comparison with radium implantation, radiotherapy and complete laryngectomy.

It is recognized that the earlier the diagnosis the better and more lasting is the result of excision by laryngofissure.

The cases in which the growth is hard, keratinized and more or less limited to the middle or anterior third of the vocal cord are most suitable for excision by laryngofissure. The commonest site for an intrinsic epithelioma of the larynx is the vocal cord and the growth tends to extend horizontally to the anterior or posterior commissure. It may burrow under the surface of the cord. A few cases commence in the subglottic area: usually near the anterior commissure and then involve the vocal cord. A slight extension upwards on to the ventricular band or into the ventricle does not make it unsuitable for successful excision. If the growth has extended to the subglottic area, the posterior commissure or across the anterior commissure with fixation of the cord it cannot be completely excised by laryngofissure. It must be remembered that the upper surface of the growth only is seen by the laryngoscopic mirror but any extension to the subglottic area though hidden can be suspected if there is any stridor, obstruction or fixation of the cord. It happens on a very few occasions that during the operation when the growth is thoroughly exposed it is found that the growth is more extensive than expected.

Gordon New of the Mayo Clinic has stated that cases which have had a laryngofissure are not such good cases for a subsequent complete laryngectomy but there is no objection to an exploratory operation by laryngofissure if there is considerable doubt as to its suitability. Direct laryngoscopy should be used in doubtful cases.

The large majority of epitheliomata can be diagnosed accurately without a biopsy. A biopsy of value demands that an adequate piece of the growth has been removed from the right place and presents a definite histological picture. Even then it is necessary to exclude tuberculosis and syphilis. It is in cases of obscure tuberculosis when the sputum is absent and when physical signs cannot be detected that a biopsy is necessary. The Mayo Clinic surgeons place considerable reliance on Broders' classification of malignancy by the histology of the section. Class 1 is comparatively benign and does not metastasize. Class 4 is very malignant. New records that all Class 4 cases found in 44 patients, in which the growth recurred after laryngectomy, died. 72% of StClair Thomson's Grade 4 cases recurred. Colledge and I have noticed that the surface of the section may be Class 1 but another and deeper part of the section may be Class 3 or 4. It is difficult, even for the expert to be reasonably sure of his classification. Moreover a larger piece than can be obtained for biopsy is essential for an accurate classification. Most of my cases free from recurrence have been of the epidermal type with cell nests and probably Grade 1.

MAY—LARYNG. 1

Finzi-Harmer and the contact therapy method published by Watson from Manchester. Adams' method approaches this minimal waste of radiation. These methods are characterized by having very few undesirable after-effects. The beam therapy method described by Lederman is intermediate between the above methods and those of deep X-ray therapy.

Accuracy of treatment is attained by care in setting up by beam direction methods such as Dobbie described or by the use of a jig as used by Wilson or, of course, more easily in the very local methods, by ensuring that the exposed field for treatment by radiation or contact X-rays covers the desired region adequately.

Choice of the best time-dosage relationship.—There are great differences here between the single dose methods, the very protracted gamma ray treatment of the Finzi-Harmer technique, and the low-intensity and high-intensity methods of beam radiation, whether by radium or deep X-ray. Thinking, as I now do, that the highest dose in röntgens, compatible with complete recovery of the normal tissues should be the aim, I believe that the best results with external radiation are likely to be obtained by using many fractionations. The rule suggested by Gray¹ that the total tolerance dose is proportioned to the square root of the number of fractionations accords with the work of Coutard and of the Beam Therapy Research, some of the best results published, in which patients were usually treated twice daily for one month. Dr. Edith Paterson's report² on the relative effects of single doses and fractionated doses on tissue cultures likewise argues for fractionation.

To avoid the ill-effects of sepsis is less easy. Recently I have been giving a full course of sulphonamides, and starting the treatment two days after this course is completed so as to avoid what I think are the undesirable effects of using radiation at the same time as sulphonamides. The first results have been encouraging. I think that the sepsis cannot, in the larynx, be adequately dealt with except through the blood-stream, and that every ulcerated cancer is infected.

¹ *Brit. J. Radiol.*, 1944, 17, 327.

² *Brit. J. Radiol.*, 1944, 17, 26.

Dr. P. C. Koller: In spite of considerable individual variations in time of appearance and degree of erythema, the conclusion that a higher dose is required to produce it by gamma radiation than by X-rays has been verified by many investigators. Accepting the fact that a difference does exist between gamma and X-rays in respect to the effects on biological material, can we attribute the difference in the tissue response to the difference in wavelength, or is it due to the low dosage rate employed in gamma ray therapy?

We must, first of all, distinguish between radiation effects induced in (1) single cells and (2) tissues.

(1) In individual, separate cells, such as sperm cells or pollen grains, the effects due to single ionizations are the same after X or gamma radiation; the difference in wavelength has no influence. Similarly when the combined effect of two or several independent ionizations, for example chromosome breaks, are considered, no significant difference between X and gamma radiation is noticeable. If there is any wavelength effect it should have been detected in properly controlled experiments on individual cells.

(2) When, however, the effects on tissues composed of cells differing in their developmental stages are studied, a different response to gamma and X-rays can be detected. It is known that cells are sensitive to radiation for a very short period during their life-cycle, which extends from one division to the next. Radiation such as gamma radiation, which is given at a low dosage rate over a long period (forty to sixty minutes) will catch more cells in the sensitive period than when radiation such as X-radiation is given at a much higher dosage rate over a shorter time (six to ten minutes). This difference can become significant in highly active tumours. Furthermore, empirical observations on skin erythema indicate that the effect on the physiological functions of normal differentiated cells is less after radiation given at low-dosage rate than at high-dosage rate: one of the results being an increase in skin tolerance to radiation.

These two effects, namely (a) higher numbers of malignant cells being irradiated in the sensitive period, and (b) higher tolerance of normal tissue, may explain the difference between gamma and X-radiation. From a biological standpoint, on account of the low dosage rate employed in radium treatment, we may consider radium better suited than X-rays to the treatment of some tumours, amongst which we can include the tumours of the larynx.

There are some points in the remarks by Mr. Davis which call for comment. Whilst it is true, as he says, that in the majority of cases a correct diagnosis can be made without biopsy, it is equally certain that in this situation mistakes will be made in cases which appear to be epitheliomatous unless biopsy is done as a routine. He says that it is in obscure cases of tuberculosis that biopsy is needed, but it is just these cases that are missed unless routine biopsy is done, because this form of senile tuberculosis in the middle-aged or elderly mimics epithelioma very closely. The majority of mistaken diagnoses are due to confusion clinically between tuberculosis and epithelioma, much less often to syphilis but also to hæmatoma, innocent tumours and leukoplakia. The latter in my view is often precancerous and justifies laryngofissure. Biopsy is not only useful in providing a confirmation of the diagnosis, but Broders' grading gives an indication of the degree of malignancy and therefore of prognosis from the surgical point of view, though at present it gives no information concerning radio-sensitivity. Any case of epithelioma in Group IV requires a very radical operation and is unsuitable for laryngofissure. Either total excision or radiotherapy by beam is the appropriate treatment. On the other hand there should be no exploratory laryngofissures, to which Mr. Davis says there is no objection. A sufficient clinical study of the case will provide the information upon which the appropriate operation can be chosen. Laryngofissure upon an unsuitable case is not necessarily a disaster, but may easily become one if the incision cuts into the tumour. In any case the best technique for the more radical operation is made impossible, and to convert the lesser procedure into the major one involves various technical difficulties.

The true tumours of the larynx, that is the intrinsic tumours which mostly arise on the vocal cords, with a few subglottic, in the ventricles or on the false cords, no longer offer any surgical problem, because appropriate operations are available for all situations and all stages short of gross extension beyond the confines of the larynx. These operations of laryngofissure, partial excision and total excision of the larynx may now be said to be standardized: the indications for each and the technique have been fully described (Lettsomian Lectures, Medical Society of London, 1943, in the press), and they provide a good percentage of lasting results. Among earlier cases out of 23 cases of laryngofissure or partial laryngectomy 18 survived more than ten years, and out of 75 cases of laryngectomy 45 survived more than ten years. As the technique is now better than it was ten to twenty years ago, and these figures include the operative mortality, the outlook now should be better than this, which gives 63% freedom from recurrence for ten years, 78% for early cases, and 60% for later cases. This percentage is so high that any form of treatment designed to replace excision must show a good record of successful results, if alternative treatment can be justified. The problem at the moment is whether radiotherapy can safely be substituted as routine treatment for these forms of cancer in place of the operations mentioned. To make the comparison Dr. Lederman will say what can be expected from radiotherapy. There are, however, a few points which need attention, because they reflect on the advantages claimed for radiotherapy. It is often suggested that as radiotherapy is a non-mutilating form of treatment it should have the first chance, because if it fails operation can follow and may still succeed. There is some truth in this and I have many patients in whom operation has succeeded after failure by deep X-rays or radium, or even both, but unfortunately it is not the whole truth. Sometimes the tissue changes after irradiation are not severe, the operative technique is not much hampered and healing is not prolonged for more than a week or ten days beyond the usual period. In consequence an experience founded on a few cases can be very misleading and cause the adoption of a too optimistic view of this situation.

In only too many cases the changes in the neck cause dissections to be extremely difficult, especially gland dissections, healing is almost indefinitely prolonged, pharyngostomes form and plastic operations on the devitalized skin of the neck fail constantly. It may be necessary to bring skin from a distance by tube pedicle grafts and relatively simple plastic operations become long, tedious and uncertain, and at the worst sloughing and hæmorrhage in the absence of the normal process of repair may destroy the patient. I do not think, therefore, that the statement that operation can follow irradiation is a valid argument for irradiation stated in that too simple form.

A further difficulty arises from the fact that the most attractive target for the radiotherapist is an early epithelioma of the cord, suitable for excision by laryngofissure. If the radiotherapist fails to cure, however, a total laryngectomy is required. I have now such a case in a robust middle-aged man who was treated by radium and then by deep X-rays. He remains well with a good pharyngeal voice after laryngectomy; but he has lost his larynx when he might have been cured by laryngofissure. On the other hand,

The anaesthesia I prefer is chloroform and ether administered by a soft small intratracheal tube. At the Mayo Clinic local anaesthesia is preferred. Five drops of a solution of cocaine injected with a hypodermic syringe through the cricothyroid membrane before splitting the thyroid cartilage results in a tranquil operation.

The isthmus of the thyroid gland was divided in all the cases so as to expose the trachea and to facilitate a tracheotomy should it be necessary. Tracheotomy has been avoided in the last 6 of the 40 cases and I now find that tracheotomy is undesirable and unnecessary. The intratracheal tube is completely reliable. As soon as the larynx has been opened the trachea is sealed by packing ribbon gauze around the intratracheal tube. This tube does not obscure the area of operation. It lies snugly on the posterior commissure and is not in any way cumbersome. My colleague L. G. Brown, who, so far as I know, first introduced the avoidance of tracheotomy, and others favour the technique.

In the remaining 34 cases the tracheotomy tube was removed before the patient left the operating table and it was never necessary to replace it.

It is essential to see that the wound is absolutely dry before the larynx is closed. Oozing is arrested by a small button electrode with the weakest possible diathermy (shortest spark gap) or by the usual method of touching the artery forceps with a diathermy electrode. Those cases in which the growth was excised by the diathermy needle appeared to me to be more septic later and took longer to heal so I have given up excision by diathermy and use the knife or scissors. New seals the laryngeal wound lightly with a small button electrode with the weakest diathermy current to be effective. Some surgeons found it necessary to use a stitch ligature for the small arytenoid artery. Hajek and J. S. Fraser packed the larynx with gauze to prevent hæmorrhage. The packing was removed the next day. This method is not recommended.

Division of the body of the hyoid bone adopted by New to allow the larynx to be drawn up into the wound and to facilitate access is unnecessary in my experience. Division of the hyoid bone causes pain and discomfort with the movement of the tongue on swallowing.

The saw, a rough surgical instrument, was not used at any time to divide the thyroid cartilage. There was never any difficulty in dividing the cartilage with the knife and Irwin Moore's shears.

I prefer to denude the thyroid alæ by dissecting off the soft tissues and growth *en bloc* and not to remove the alæ. The thyroid cartilage is a barrier to the spread of the growth. There has been no disadvantage when the thyroid alæ have been removed.

At the end of the operation the thyroid alæ are accurately replaced and the larynx closed by fine catgut stitches through the thyrohyoid and the cricothyroid membranes.

There were no deaths as the result of the operation in the 40 cases. The mortality in 41 operations performed by Gordon New was nil. It is interesting to note that in 1888 before the days of sepsis and antisepsis Morel Mackenzie reported 22 cases, 6 of whom died and 72% recurred.

Deep X-ray with teluradium (radium bomb) in my experience has been unsatisfactory. Burning of the skin and necrosis of the cartilage and even the rings of the trachea have caused misery to the patient. Two cases of early intrinsic carcinoma of the vocal cord treated by teluradium with recurrence after two years were treated by laryngofissure and were still without recurrence after five years.

Radium implantation gives the most beneficial dose at the right spot more accurately than any other method of radiotherapy but my experience of this technique is too small to be of any value.

Laryngofissure.—Gordon New: 41 cases, 13% recurrence. StClair Thomson: 60 cases, 25% recurrence. Davis: 9, no recurrence after five years and longer; 5 recurred after two years; 4 recent operations within two years; 7 exploratory and unsuitable; 15 cannot be traced.

Laryngectomy.—Mayo Clinic: 86 cases, 52% recurrence; 8% immediate mortality.

Radium implantation.—Harnier (personal communication): 24 early cases, 14 survived three years, 42% recurrence; 72 advanced cases, 32 survived, 54% recurrence.

Lionel Colledge: Mr. Davis seems to think that I always excise the larynx. But there is no real contrast between laryngofissure and total excision of the larynx. The proper operation must be selected for each case. The operations to be employed are: laryngofissure, a partial excision which rather goes beyond the limits of strict laryngofissure, and total laryngectomy. I have already described the technique, most recently in the Lettsomian Lectures delivered before the Medical Society of London, and I do not think I need detain this meeting with detail, because I look upon the operations as more or less standardized.

therapy with greater technical precision and flexibility and permit greater individualization of treatment than is the case with X-ray therapy.

For the individual case of intrinsic carcinoma of the larynx the selection of treatment method as between surgery and radiotherapy is difficult. Whilst it is obvious that there is need for both methods if all patients are to receive the best treatment, there is a diversity of opinion concerning the precise indications for each method. Any attempt made to solve this problem must take into account the following considerations:

General condition of the patient.—Age and general condition do not limit radiotherapy to the same extent as surgery. The modern treatment of laryngeal cancer is one of the mildest of all curative radiotherapeutic procedures. Correctly administered treatment should not give rise to any general constitutional upset, and local symptoms need rarely exceed increased huskiness accompanied by slight soreness or dryness of the throat. Severe dysphagia or marked skin reactions should not occur, and in most cases oedema of the larynx is avoidable.

Purpose of treatment.—If on any grounds, either general or local, curative treatment is out of the question it is evident that radiotherapy can offer more than surgery. The only palliative procedure available to the surgeon is tracheotomy, whereas the radiotherapist can often relieve distressing symptoms and prolong the life of the patient in reasonable comfort. Frequently the assistance of both is required.

Histology of the tumour.—It is not uncommon to find, particularly in American literature, considerable importance attached to the histological grading of squamous cancer. This method of grading is of some value in assessing the degree of malignancy and also the method of treatment in so far as the more anaplastic types, i.e. Grades III and IV, are usually biologically inoperable even when technically operable. Grading may also assist in prognosis, but it provides little guide to radio-sensitivity, since anaplastic carcinomata are not necessarily, as is often assumed, more radio-sensitive than differentiated carcinomata.

Extent and site of the disease.—The extent of the disease is clearly of paramount importance in selecting treatment. The degree of laryngeal extension and the presence of extralaryngeal spread or metastases will frequently decide whether surgery or radiotherapy is to be employed, and, in the case of the latter method, whether treatment is to be purely palliative or not.

Site is equally of importance since supraglottic neoplasms, arising from the ventricle, the false cord or the base of the epiglottis, tend to be most, and the subglottic neoplasms least, radio-sensitive, with tumours of the true cord showing an intermediate and moderate degree of radio-sensitivity. Hautant recommends radiotherapy for most of the supraglottic, and laryngectomy for some of the ventricular and all the subglottic neoplasms. Although experience proves that the supraglottic tumours are a satisfactory group to treat by radiotherapy, opinions as to the suitability of the subglottic group for radiotherapeutic treatment should be accepted with reserve until radiotherapists are given greater opportunities of treating them. It is the common tumour of the true cord which presents the greatest problem. I believe that cancer of the true cord should always be treated by radiotherapy, with the exception of the more advanced and some of the recurrent cases. A certain number of advanced cases showing fixation of the cord can be cured by radiotherapy, but the presence of infiltrated cartilage reduces the prospects of cure, whilst a complicating septic perichondritis is an absolute contra-indication to radiation.

Where doubt exists as to the best method of treatment trial radiation is justifiable. By this means it is possible to determine approximately whether a particular tumour will or will not respond before a full course of treatment is given, and if necessary surgery can be undertaken before marked radiation changes occur in the tissues. Features suggesting that radiotherapeutic treatment should be abandoned or given for palliative purposes only are: (a) Poor response of the primary lesion, or no improvement of symptoms such as dyspnoea and stridor at the end of half the course of treatment—roughly three weeks. (b) A laryngeal oedema which fails to subside during treatment, or an oedema arising early in treatment and persisting. (c) Local septic complications as shown by: (i) Persistent pyrexia in the absence of an extralaryngeal focus of infection; (ii) the onset during treatment, or persistence, of fœtor; (iii) perilaryngeal abscess. (d) any deterioration of the patient's general condition, particularly loss of weight in the absence of dysphagia.

It is difficult to lay down any hard and fast rules for the treatment of recurrent cases. For local and scar recurrences after excisional surgery radiotherapy is useful as a palliative agent and sometimes effects a cure. We have had more success with post-laryngectomy recurrences than with those following laryngofissure: radical surgery should be considered for the latter if the aim is cure rather than palliation.

a spare, elderly man came to me with an early epithelioma of one cord, very suitable technically for laryngofissure, but he has a high blood-pressure and has lost the sight of one eye from a detachment of the retina. These may not be absolute contra-indications to operation, but I regard them as relative contra-indications when the alternative of radiotherapy is available. Dr. Lederman restored the larynx of this patient to a normal appearance, and so far it has remained so, but only a year has elapsed. In another case a well-preserved man over 80 has had a normal larynx for more than a year since an epithelioma of the anterior commissure disappeared under the influence of telradium. I particularly mention these early cases which provide a brilliant success to the radiotherapist, because the more the growth has advanced the more difficult becomes his task and the greater the percentage of failures. Consequently radiotherapy is not complementary to excision, but is only an alternative method. In other words, radiotherapy is a much more efficient substitute for laryngofissure than it is for laryngectomy, which is naturally the more mutilating operation. I feel, therefore, that whilst selected cases should be treated by radiotherapy, it is not right to treat all cases as a routine by radiotherapy and operate afterwards on the failures. Biopsy does not help to distinguish the tumours which are likely to prove failures from those that are radio-sensitive, and the therapeutic test which has been proposed by Nielsen and Strandberg, 1942, *Acta radiol. Stockh.*, 23, 189, and Cutler, 1944, *Arch. Otolaryng., Chicago*, 39, 53, seems to me to indicate a half-hearted, undecided attitude. It is still necessary to consider each case as a whole and then decide whether to recommend excision or radiotherapy for that individual.

Finally, the time has passed for burying needles in the neck. If radiotherapy is employed it should always be by means of the telradium beam, which can now be adjusted to such accurate dosage that the risk of radionecrosis is very small, provided the patient is protected from minor injuries locally.

M. Lederman: *Treatment by radiation of the so-called intrinsic cancers of the larynx*, that is, primary squamous cancer arising from: (1) The ventricle, the false cord, and the base of the epiglottis; (2) the true cord; (3) the subglottic region. Extrinsic cancers have been excluded because they are pharyngeal in origin and require an entirely different radiotherapeutic approach.

Two main radiotherapeutic methods are available for treating intrinsic cancer: (1) The use of radium either alone or in combination with surgery, e.g. telradium or the Finzi-Harmer operation. (2) The use of X-ray therapy either alone or in association with surgery, e.g. high voltage therapy or the Lambert-Watson operation, which is roughly the X-ray counterpart of the Finzi-Harmer operation.

A combination of high voltage X-ray therapy and telradium finds favour at some centres. The intralaryngeal use of radium either by intubation or implantation of radon seeds and the use of surface radium moulds are to be condemned.

The Finzi-Harmer and the Lambert-Watson procedures find their greatest field of usefulness in the treatment of early lesions of the vocal cord, i.e. the type of case for which the laryngofissure operation is available. High voltage therapy or telradium can be used for similar cases as well as the more advanced cases which surgically would demand partial or total laryngectomy.

Whilst the Lambert-Watson procedure is too recent for its value to be assessed, the Finzi-Harmer operation represents a definite landmark in the history of radiation treatment of endolaryngeal cancer, and its value has been established beyond all reasonable doubt. Nevertheless, I believe that external radiation by telradium or high voltage X-ray therapy can and probably will supplant this method for the following reasons: (1) The results obtained by external radiation for comparable cases are as good without any operative risk; (2) on physical grounds external methods are more efficient and safer; (3) individualization of treatment is the keystone of success when dealing with a group of tumours of variable and unpredictable radio-sensitivity. The necessary degree of individualization is only possible with external radiation, where the treatment can be clinically adapted to a particular patient's requirements, in contrast to the Finzi-Harmer method where the patient has to be submitted to a fairly rigid technique.

Fundamentally the only difference between gamma rays and X-rays is one of wavelength, and whether the short wavelength γ -rays differ from the longer wavelength X-rays in their biological effect on malignant tissues is still not definitely known. Upon purely clinical grounds I am convinced that normal tissues, dose for dose, show less change with telradium than with X-ray therapy under ordinary conditions of treatment. This may, however, be due to the different dosage-rates employed rather than to any difference in wavelength. Certain differences of apparatus and physical conditions of treatment endow telradium

TABLE II.—CASES TREATED AT THE ROYAL CANCER HOSPITAL (1933-1944 INCLUSIVE).

Total cases	Material	Survivals	Dead		
			Disease present	Untraced	Inter-current disease
56		18	3	1	1
All cases seen were treated	Operable 23	8 : 5 yrs. or more			
Teleradium used exclusively	Inoperable 19	1 : 5 yrs.	15	3	—
	Recurrent 14	5 1 : 5 yrs. or more	8	—	1

TABLE III.—ROYAL CANCER HOSPITAL OPERABLE CASES TREATED BY TELERADIUM THERAPY.

Operation	No. of cases	Result
Suitable for : Laryngofissure	4 } 8	All patients initially symptom-free
Partial laryngectomy	(5 patients between 72-79 yrs. of age)	6 living and symptom-free : 2 for 5 yrs. or more 1 for 2-3 yrs. 3 for 1-2 yrs. 1 patient died of intercurrent disease 1 patient untraced
Suitable for laryngectomy	15	12 living and symptom-free : 6 for 5 yrs. or more

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Lieutenant-Colonel W. L. Harnett (*Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign*) brought forward some as yet unpublished figures concerning 123 cases of cancer of the intrinsic larynx. There were 113 males and 10 females, a sex ratio which was in accord with general experience. The mean age in both sexes was 62. On a clinical classification there were 57 early cases, in which the disease was confined to the larynx, 63 advanced cases in which it had spread to the surrounding tissues, with or without metastases in regional lymph nodes, and 3 cases in which there were distant metastases. Of the 57 early cases, 15 were treated by radical surgery, of whom 13 were alive after four years, 19 by radium of whom 8 were alive, 13 by X-rays of whom 4 were alive and 10 by palliative methods, all of whom were dead. The operation mortality for laryngofissure (12 cases) was 8.3%, for laryngectomy (3 cases) nil. Of the 66 patients in the later stages all except 5 were dead.

E. Musgrave Woodman said that he did not agree with Mr. Colledge that to bury needles in the neck was an anachronism. He followed Mr. Douglas Harmer in using needles with the window method for the treatment of carcinoma of the vocal cord. It was unfortunate that Mr. Harmer had not been able to be present because that particular method of application had not been presented. Carcinoma of the vocal cord itself could be cured by operation or by radiotherapy. Excellent results were obtainable with laryngofissure, and Mr. Harmer had obtained excellent results with radium therapy. The speaker had hitherto followed the method of inserting radium needles through the window in the larynx, and if necessary following it up with X-radiation through the port thus made. The results had entirely satisfied him.

Even if the result with radiotherapy was constantly no better than that with surgery they must, in fairness to their patients, use radiotherapy because it restored the larynx to the condition in which it was before; in other words, the patient had a good voice, whereas with the best of operations there was a defective voice. He had been rather disturbed by the inefficient result of radium on growths in the sac of the larynx and at the base of the false cords. In his experience not one such case had done well with radium or teleradium, but such cases should be sharply separated from primary growths of the cord, and should be first subjected to surgery as the method of choice, followed later, if necessary, by radiotherapy.

For local recurrences after radiotherapy it can be stated quite categorically that further radiotherapy has many dangers and only infrequently results in cure: wherever possible these cases should be treated surgically; failing this radiotherapy can be undertaken as a palliative treatment.

The best way of dealing with cervical lymph-node metastases is as yet undecided. In a previously untreated neck I recommend telerradium as the primary method of attack in both operable and inoperable cases, surgery being retained as a second string. If metastases occur in a previously treated neck, surgery should, if possible, be the first choice and radiotherapy reserved for cases unsuitable for this method.

Any claim made for the wide use of radiotherapy in the treatment of operable intrinsic laryngeal cancer, to be acceptable, must be based upon the results obtained. It is therefore of the utmost importance that the following facts be given due consideration when attempting to assess and compare radiotherapeutic results with those of surgery:

(1) Surgical skill and technique in the performance of the various laryngeal operations for cancer have reached their peak of efficiency and it is unlikely that any further developments of technique will produce much improvement in results. By comparison radiotherapeutic treatment is still in process of development and has, in fact, only recently emerged from that dismal stage wherein laryngeal surgery found itself fifty years ago.

(2) Figures emanating from surgical sources are selected figures since only cases operated on are recorded. To obtain an accurate picture of the true value of the method as much attention should be given to the number of cases found unsuitable for surgery as to the cases successfully treated.

(3) The radiotherapist has to be content to base his results largely on material discarded by the surgeon. A true comparison of results will only be possible when the radiotherapist's material is comparable.

(4) There is no statistical method of showing the two great advantages of radiotherapy over surgery, namely, conservation of the larynx and the absence of an operative mortality.

The results of surgery are on the whole very good and are a credit to surgical skill and achievement. In Mr. Colledge's series, for example, 70% and 60% ten years' survival rates set the radiotherapist a very high standard for emulation but the operative mortality and recurrence rate for most published series are not negligible.

I believe that Tables I, II and III provide enough evidence to show that for the early cases, i.e. those suitable for laryngofissure or hemilaryngectomy, radiotherapy can offer the patient as much as surgery with less risk. Similarly for the more advanced cases where laryngectomy is the operation of choice radiotherapy can successfully compete with surgery in an appreciable proportion of the cases, but there will always be a certain number of patients who will have to sacrifice the larynx to save life. For the inoperable cases radiotherapy is of palliative value and shows on the whole a worth-while salvage rate.

The figures also show that radiotherapy results are durable. My own experience leads me to believe that the case that does well initially remains well, i.e. the recurrence rate is not high, certainly less than that following surgery.

The radiotherapist is dependent on his surgical colleagues for material and unless he is adequately supplied with suitable cases radiotherapeutic progress is bound to be painfully slow. The problem of the "relative spheres of interest" of radiotherapy and surgery could be settled within the next decade were the radiotherapist enabled to explore fully all the promising potentialities that radiotherapy possesses.

Slides were shown illustrating radiation reactions, results of radiation treatment and types of case both suitable and unsuitable for radiotherapy.

TABLE I.—RESULTS OF RADIOTHERAPEUTIC TREATMENT.

Author	No. of cases	Material	Survival rate	Period of observation
Coutard (1921-32)	143	Precise details not stated. Mostly inoperable and post-operative recurrences	30 = 27%	5 years
Schintz and Zuppinger (1929-35) ...	33	Operable and inoperable	4/14 = 28%	5 years
Nielsen and Strandberg (1931-40) ...	63	Operable 20 Inoperable 43	6/10 = 65% 8/32 = 25%	3 years
Cutler (1938-43)	84	All cases Cord tumours : Mobile } 28 Partly fixed } Fixed } 12 40	31/84 = 37% 23/28 = 82% 0/12 = 0%	3 years
			23/40 = 57%	
Blady and Chamberlain (1931-37) ...	23	No precise details but of 11 patients with cord fixation 5 survived 5 years	13/23 = 67%	5 years

radiotherapists that it was more scientific to use external radiation, but certainly the cases he had treated by implanting radium needles by the Finzi-Harmer method had done very well. They had a brief time in bed, with little suffering, and they had the advantage of the removal of the cartilage so that there was no irradiation through the cartilage, and there should therefore be no perichondritis.

C. P. Wilson said that though he had had the advantage of being associated with a first-class radiotherapeutic department, he had never seen radiotherapeutic results as good as those he had just heard about, nor had he ever seen surgical results which approached the results one heard about.

From the statistical point of view it would be interesting if some of their statisticians could take the figures which had been given by the first three openers and set them out on the basis which Colonel Harnett had given.

Concerning surgery following radiation there was one point he desired to make, namely, that surgery should never be attempted after a patient had had more than one course of radiation. From his own limited experience he would say that surgery was quite impracticable when there had been extensive radiotherapy. From the point of view of assessing cases suitable for one or other method of treatment he did not think they could go further than Mr. Negus had already gone. He knew of no method by which the cases likely to prove radio-sensitive could be assessed with any degree of probability.

L. Graham Brown said that he had seen a great number of cases of carcinoma of the larynx, but he had confined his operative procedure to simple carcinoma of the cord, preferring to refer other cases to radiation.

They were agreed that laryngofissure was a simple operation and a very successful one. Concerning the other cases, considerable differences were noted; sometimes the result was marvellous and at other times most depressing, but he thought that there was a great future for radiotherapy in these cases. It depended a great deal on whether they could get proper standardization of treatment.

He remembered in that Section some years ago drawing the fire of the late Sir StClair Thomson because he had not done a preliminary tracheotomy in cases of laryngofissure. He thought that with the great advance in technique, with the added benefits of intubation, and also with the use of the diathermy or cautery point, bleeding could be sufficiently controlled to get a dry field often without preliminary tracheotomy. He thought that this practice applied also in America to a considerable extent. A tracheotomy did retard the convalescence. In a recent case, after performing a successful operation of laryngofissure, feeling he should give the patient the benefit of the doubt, he sent him for a course of radiation. Unfortunately, although the patient made a quick recovery from the operation, he suffered for months afterwards from the radiation treatment.

Colonel N. Canfield (U.S.A.M.C.) said that he wished to mention that their war surgery during the last six months had shown the value of tracheotomy in treating wounds of the larynx, pharynx and jaws. Tracheotomy diminished the muscular action of the pharynx and larynx and these cases healed very much better. He thought this might possibly apply to cases in which a tracheotomy had been performed in preparation for laryngofissure.

E. D. D. Davis, in reply, said that the Harmer-Finzi operation appealed to him because it gave the right dose at the right spot. Mr. Harmer and his colleagues had worked out the technique very thoroughly. Teleradium and X-ray therapy produced burning and considerable skin irritation and discomfort. Two cases of laryngofissure in which it was thought the growth had not been completely eradicated were given teleradium as a prophylactic treatment. Both patients died of secondary growths of the liver within twelve months.

Lionel Colledge, also in reply, said that he had been sorry to hear that Mr. Musgrave Woodman was so "reactionary" on the subject of treatment by radium needles. It could not be anything like so scientifically accurate as teleradium, and the results which Dr. Lederman now obtained showed that teleradium treatment produced everything, in selected cases, that could be produced by other procedures. On the other hand, Dr. Lederman and Professor Mayneord had shown that if radium needles be used as the source of irradiation in the larynx the distribution in the horizontal plane shows a region of heavy irradiation at the anterior commissure, but falling off rapidly along the cord in

Mr. Colledge had been a pioneer in laryngectomy, and his results were excellent. But it was rather difficult to persuade a patient to give up his larynx and to be told that he would never speak again. If any method could be found which would remove that unpleasant necessity they would all be pleased.

He had been interested in one of Mr. Davis's cases which had died of carcinoma of the œsophagus. One of his own best cases had an extensive growth in the larynx and pharynx. He had had to take out the larynx and pharynx, but the patient lived for ten years and then developed cancer of the œsophagus and died therefrom.

N. S. Finzi said that when they saw a patient with an intrinsic growth of the larynx the best thing they could do was to put themselves in his position, and, knowing all they did about the various treatments, imagine what they would desire in their own case. As to growths which were suitable for laryngofissure, they had to consider the patient's life first rather than his voice. There was no question about the effect on the voice; Mr. Harmer had had gramophone records of voices made, and the comparison between even the best "laryngofissure voice" and the average "radium voice" was very striking. Some of Mr. Harmer's cases had survived for over twenty years.

From what Mr. Lederman had said it looked as if telerradium was going to give better results than radium implantation. If subsequent operation were necessary, however, the cases in which implantation had been used would not give anything like the difficulty which might be expected in cases receiving external radiation. On the other hand, if anything like as good results could be obtained with external radiation, this should be given.

Treatment by radium in former times did not afford such good results as were obtainable when individual treatment was developed later. He thought there was likely to be further improvement in results now that sepsis could be so largely eliminated. Though operations were sometimes necessary for the failed cases of radium and X-ray treatment, there were also, of course, the failures of surgery with which radiotherapists had to deal.

The speaker suggested that Mr. Davis might have got better results if he had had these cases heavily irradiated after laryngofissure in order to prevent that small percentage of recurrences in those cases where he had failed to remove the growth completely. Mr. Lederman had shown some cases where there was an unexpectedly large spread of the growth beyond that visible with the laryngoscope and he had himself seen some of these cases. Perhaps it might help to eliminate some of the errors if a skiagram of the soft tissues were taken before treatment was started.

V. E. Negus said that about five years ago the late Sir StClair Thomson and himself started to write another edition of the textbook, and now, after Sir StClair's death, he was left to carry on that struggle alone. It was very difficult in editing such a book to form conclusions as to the right treatment of certain diseases of the nose and throat. He had found this particularly when endeavouring to decide what was best for a patient who had carcinoma of the larynx. If they could get patients cured by radiotherapy, with a normal voice afterwards, instead of by operation, with a somewhat hoarse voice, they should certainly do so; but he had had a certain number of patients with a type of growth which might be expected to respond to radiotherapy who came back with recriminations because they had been subjected to that procedure. He warned patients that they must not expect that they were going to get off lightly by avoiding an operation and having radiotherapy instead. Some patients said afterwards that they had suffered considerably as a result of the prolonged treatment and the reaction; he had not had the same recriminations in the case of patients on whom he had operated.

In a few cases patients a year or two later had perichondritis after external radiation. (He was talking rather about deep therapy, not telerradium, but he understood that there was not very much difference between the two methods.) Those cases were very depressing. If a patient had a growth of low-grade malignancy and of suitable distribution, he would at present recommend laryngofissure because of these reactions. If irradiation technique improved, and these subsequent reactions were avoided, he might alter his opinions.

He did not think that laryngectomy was a difficult or dangerous operation, but he had found difficulty with a considerable number of patients in getting them to adapt themselves to their life afterwards. The hypertrophic laryngitis which went on to carcinoma should be treated by operation and so should cases with perichondritis. But if there were a carcinoma along the whole of one cord, extending to the posterior commissure, when surgical treatment would necessitate laryngectomy, the patient might be given the chance of radiation treatment. He had been told on the authority of

Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[February 6, 1945]

DISCUSSION ON TREATMENT OF UNILATERAL OSTEOARTHRITIS OF THE HIP-JOINT

Mr. G. R. Girdlestone (*Pseudarthrosis*) began with an expression of his opinion that the surgical treatment of osteoarthritis of the hip was only indicated when, in spite of all that could be done by conservative treatment, pain was severe and the disability as a whole badly handicapped the patient's activity and enjoyment of life.

His second point was a reminder that the best we could do was so far behind the combination of free movement and stable function of a normal hip that it was unjustifiable to subject a patient to operation unless one took every possible step to ensure the very best result that could be achieved. This meant that operations for osteoarthritis of the hip should be confined to hospitals where everyone concerned with the operation and the subsequent treatment was a member of a skilled and experienced team. It was an absolute necessity that every patient should clearly understand what was to happen to him and what result he could look forward to.

In his view every orthopædic surgeon should make himself expert in the technique of the best operations required for this condition; and it was for the surgeon to discuss with the patient alternative methods, what they necessitated, and what advantages they offered. As an illustration he had collected from the Wingfield-Morris Orthopædic Hospital's records a series of operations for osteoarthritis of the hip performed by his colleagues and himself: Pseudarthrosis 44, arthrodesis 24, arthroplasty 12, osteotomy 13, "reconstruction" 6, various 11. Total 110.

In a series of 25 cases in which he had performed pseudarthroses in the years 1924 to 1940 inclusive, there was no mortality: The average age at operation was 57; ascertained end-results in 22¹, at an average period after operation of nine years. Results: Excellent 14²; good 5; poor 3.

Though some disappointments in this field were inevitable as it was made up of an elderly age-group the results on the whole were encouraging, the first patient in the series, twenty-one years after his operation, and now aged 76, still walks ten miles a day and works hard in his garden. Another mentions shooting, tennis and dancing. The oldest, now 79, goes to his office in Trafalgar Square every day, travelling by train to Waterloo and thence by Underground, during the rush hours.

Mr. Girdlestone then described some points in the surgical technique and after-care which he regarded as of special value and importance.

Mr. R. Watson-Jones: *Nail arthrodesis for unilateral osteoarthritis of the hip-joint.*—The literature of the last twenty years proves the failure of arthrodesis of the hip-joint if reliance is placed on the simple technique of denuding the joint of articular cartilage and immobilizing it in splints or plaster (see Bristow (1927), 30 cases; Ozarki (1917), 26 cases; Spiers (1920), 34 cases; Max Page (1924), 34 cases; McMurray (1939), 10 cases; and Plewes (1939), 7 cases). In all these cases there was bony union in only 40% of attempted fusions. Moreover, consolidation was so long delayed that whether it was ultimately achieved or not, deformity very often developed and the functional result was poor; in one series there was adduction deformity in 80%. Finally, since unsound ankylosis caused protective muscle spasm, deformity of the hip, and therefore low back strain, backache was a persistent symptom. In these circumstances it is not surprising that arthrodesis of the hip-joint fell into disfavour.

Reason for the failure of arthrodesis of the hip-joint in former years.—This low proportion of successful fusions after arthrodesis of the hip-joint is almost identical with the proportions of successful union after the Whitman spica treatment of fractures of the neck of the femur—again an average of 40%. The proportion is similar because the problem is the same. Whether bone union is expected in the neck of the femur, or in the hip-joint itself, a simple plaster spica is inadequate because: (1) A spica does not completely prevent angulatory and rotatory strain so that consolidation is delayed or prevented; (2) a plaster spica cannot be kept in position for the many months or even years which may be needed to achieve firm consolidation. The introduction by

¹ Three others have disappeared, all were doing well when last seen but are not included.

² Two patients who died more than twelve years after the operation are included.

the direction of the arytenoid cartilage. Morton, Gray and Neary also found by physical measurements that by the usual method of employing needles the anterior part of the larynx receives twice the dosage that reaches the posterior part. Therefore it is only a very small tumour which can receive a homogeneous dosage.

Much had been said about the loss of voice following laryngectomy. But this loss was not complete, and in some cases the patients held their own very well. He had in mind a solicitor, aged about 50, who had managed to conceal from everybody except his own doctor the fact that his larynx had been excised. He was a little husky, but no one in his own town knew that he had undergone an operation. With the co-operation of a speech therapist, the speech difficulty was no longer to be accounted among the disadvantages of the operation.

Dr. Finzi had suggested that the operations which followed radiation were more difficult if telerradium had been used than if the radiation had been applied by means of needles. On the other hand, there was a good deal of scarring in the neck if needles had been implanted, and, worse still, the cartilage on one side had been removed prior to the spread of the tumour. It had been his experience that operations had been more difficult after needling than after external radiation.

Mr. Graham Brown and some others were inclined to condemn tracheotomy as a first step. But in laryngofissure now and then the patient did bleed severely a few hours after the operation, and tracheotomy was a safeguard.

REFERENCES

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MORTON, J., GRAY, L. H., and NEARY, G. J. (1944) *Brit. J. Radiol.*, 17, 204.

T. B. Jobson asked whether Dr. Lederman was of opinion that the preliminary removal of cartilage on the side of the growth would increase the penetrative power of the rays and lessen certain risks.

M. Lederman, in reply, said that in his view the removal of the cartilage would not be of any value and would certainly not affect the penetrating power of gamma radiation. Hautant in Paris at one time removed part of the thyroid cartilage, but the procedure had since been given up.

Replying to other points in the discussion, Dr. Lederman said that Dr. Finzi had mentioned the expediency of taking a soft tissue skiagram in these cases. That was done, plus tomography, in the cases he had described.

Mr. Negus and Mr. Davis had mentioned reactions. He had been at some pains to investigate this point. With telerradium the reactions were never as bad as had been supposed.

External radiation was the only method whereby the right dose could be introduced to the right spot. The whole weakness of the Finzi-Harmer method was that there was a tendency for a very large dose to be delivered to the anterior commissure, and only half that dose to the region of the posterior end of the cord.

Results of nail arthrodesis of the hip.—If the subject of discussion had included bilateral osteoarthritis of the hip-joints there would have been much debate on the part to be played in treatment by arthrodesis. It is true that arthrodesis of the joint in which arthritis is most advanced could be supported on the grounds that if one hip is strong and painless the other can be protected. But the alternative claims of arthroplasty of one or both joints by fascial interposition, insertion of a vitallium cup, or excision of the head and neck of the femur, must be weighed carefully when the problem is that of two painful stiff hips. All arthroplasties in the table below were performed for bilateral osteoarthritis.

ANALYSIS OF 326 PERSONAL OPERATIONS FOR ARTHRITIS OF THE HIP-JOINT.

Arthrodesis of hip	185	McMurray osteotomy	30
With graft... ..	50	For osteoarthritis	13
With nail	135	For ununited fracture	17
Arthroplasty of hip	29	Trochanteric osteotomy	82
With fascia	10		
Vitallium cup	6		
Excision head and neck	8		
Pseudarthrosis	3		
Acetabuloplasty	2		

But the discussion is limited to unilateral osteoarthritis of the hip-joint and in these circumstances I suggest that all doubt is removed. A patient with one hip-joint soundly ankylosed in the optimum position, who in every other respect is normal, has so slight a disability that he passes as a normal individual. He has no pain; he has no appreciable limp; he can walk ten or fifteen miles with ease; he can run and jump; he can play games and climb mountains; a man can go back to strenuous labour; a woman can do household duties; she can climb ladders and scrub floors. One patient with an arthrodesed hip-joint is a plate-layer on the railway; he walks 10 miles every day of his life; another is a railway porter; one drives a two-seater car hundreds of miles a week; another used to ski every winter; a lady of 60 went tobogganing within eight months of arthrodesis; her only complaint was that she found it difficult to balance near a precipice! Are these results to be compared with those of arthroplasty? A patient with a vitallium cup may demonstrate free movement when lying on a couch, but can he jump from a five-barred gate? Would he dare to do so? In considering the results of excision of the head and neck of the femur we have heard that most patients rely on walking sticks but some learn to discard their surgical appliances. Walking sticks? Appliances? The patient with a sound arthrodesis would be insulted by the offer of a stick; it would never occur to him to use an appliance. The functional result is so excellent that no arthroplasty, pseudarthrosis or bifurcation osteotomy is to be compared with it.

Disadvantages of arthrodesis of the hip-joint.—(1) *Severity of operation:* The operation is one of some magnitude; it takes at least two hours to perform both stages and apply a plaster spica. One early case in this series died of post-operative shock. But that was ten years ago; it was before I introduced the two-stage operation; it was before blood and plasma transfusions were readily available; it was in the days when even a single pint of blood was given only after the emergency had arisen. During the last few years we have learned to control shock. A plasma drip is started at the beginning of the operation and a ten-minute pulse and blood-pressure chart is kept; by suitable control of the rate of drip it is possible to prevent any semblance of shock. In patients of 30 to 35 years whose arthritis is due to traumatic dislocation or congenital subluxation both stages can be performed in one operation. Even in patients aged 55 to 75 with a two-stage operation there is no greater risk than with any major procedure. Among 70 patients in this series whose hip-joint was arthrodesed for degenerative osteoarthritis the youngest was 40 years and the oldest was 74. The average age was 46.1 years; one died on the tenth day from paralytic ileus; in no other patient in the series, of over 300 operations did the question of operative mortality arise.

(2) *A stiff hip is not ideal:* When the procedure is described as "a stiffening operation" the patient may well reflect "My hip is stiff now; whatever will it be like after a stiffening operation?" But the fact is that arthrodesis does not make the joint any stiffer than it becomes without treatment. Moreover, so far as the patient is concerned the hip is not stiff; by virtue of pelvic movement there appears to be 40 or 50 degrees of flexion movement and at least 30 or 40 degrees of adduction-abduction movement. To describe the procedure as "a stiffening operation" is to convey a false impression. If the surgeon actually demonstrates the ultimate range of movement patients do not take exception, particularly since the operation is seldom suggested except for a joint which is already stiff.

Smith-Petersen (1931) of the three-flanged nail removed both difficulties: (a) The length of the nail prevented angulatory movement and the flanges prevented rotatory movement; (b) the nail could remain in the bone indefinitely so that fixation was maintained for months or years without hardship to the patient. This was so clearly the solution not only to the problem of fracture of the neck of the femur but also to that of arthrodesis of the hip-joint that I first performed a nail arthrodesis in 1931—the same year that Smith-Petersen described the nail. In 1934 I reported 16 cases, in 1938 50 cases, and to-day 185 arthrodeses of the hip-joint, 50 with ilio-femoral grafts for tuberculous or septic arthritis, and 135 with three-flanged nails for degenerative osteoarthritis.

Technique of nail arthrodesis.—The two essential steps of the operation are: (1) To denude every shred of articular cartilage from the acetabulum and femoral head, and break up and fragment the rawed surfaces; (2) to drive a three-flanged nail from below the trochanter into the thick bar of iliac bone which runs from the acetabulum to the sacro-iliac joint. Through a Smith-Petersen exposure the joint is dislocated by dividing the capsule and rotating the femur outwards; the rotation is then increased to about 150 degrees from the neutral position so that the acetabulum is fully exposed. When all cartilage has been removed the freshened surfaces are roughly broken up with a chisel, the head of the femur is replaced and the wound is sutured. If it is performed skilfully this first stage of operation can be almost bloodless; it causes less hæmorrhage and less shock than a trochanteric osteotomy. For the second stage the patient is fixed on a traction table with the limbs in neutral rotation and the malleoli just touching; there must be no more abduction of the arthritic hip than is necessary to correct true shortening. The limbs remain fixed in the corrected position throughout the nailing procedure. It is true that lateral radiography is then impossible, but in contrast with the operation of nailing a fractured neck of the femur lateral radiography is not essential; if the nail is correctly placed in the anteroposterior plane there is a very wide margin of error in the lateral plane. On the other hand if the normal limb is fully abducted in order to permit lateral radiography there is danger of tilting the pelvis, thus causing abduction deformity of the nailed hip with apparent lengthening and low back strain. The ultimate result is so dependent on sound fusion in the optimum position that it is essential: (1) To fix both limbs on a traction table (but with minimal traction so that the head of the femur is not distracted from the acetabulum); (2) to hold the limbs in neutral rotation, with the malleoli just level, and with no deliberate flexion (the patient lies with slight lordosis which gives the optimum flexion deformity of 30 to 40 degrees); (3) to keep the limbs fixed in this position throughout the operation. A nail of the correct length (usually $4\frac{1}{2}$ in. but subject to radiographic control) is introduced through a lateral incision over the trochanter. A plaster spica is applied for ten weeks.

The advantage of nail arthrodesis over arthrodesis with graft.—Combined intra- and extra-articular arthrodesis with an ilio-femoral bone graft causes more hæmorrhage and shock than a nail arthrodesis. Moreover an ilio-femoral graft arthrodesis cannot readily be performed as a two-stage operation, whereas with nail arthrodesis in elderly patients an interval of two or three weeks may elapse between the two stages. Each stage can be completed within thirty to forty minutes and is a much less formidable undertaking than extra-articular arthrodesis. Finally nail arthrodesis is preferable to graft arthrodesis because after the plaster is discarded at the tenth week the strength of the nail must be relied upon for continued immobilization. An arthrodesis is seldom if ever consolidated by bone in ten weeks; it may not be soundly consolidated even in ten months; reliable fixation must be continued for as long as twelve months to two years if deformity is to be prevented. Indeed it is probable that occasionally the joint never consolidates soundly by bone; but even in such a case the ankylosis which develops, *together with the fixation of a three-flanged nail*, is sufficient to be the clinical equivalent of bony ankylosis. The reliability of nail arthrodesis is therefore more certain than that of any other operative fusion of the osteoarthritic hip-joint.

The failure of fusion by nail alone.—At one time it was thought that it might be enough in elderly patients to drive a three-flanged nail into the pelvis without exposing the joint and removing the cartilage. The results at first appeared to be satisfactory (Burns, 1939). But experience has shown that unless a hip-joint is already very stiff, and indeed almost completely stiff, the fixation of a nail is not sustained; painful rocking movement develops between the femur and nail, and between the nail and pelvis. These cases are significant not only because they show the failure of fusion by nail alone, but because they indicate the possibility of failure even after the full operation unless the nailed hip is protected during the first two or three months by means of a plaster spica.

Results of nail arthrodesis of the hip.—If the subject of discussion had included bilateral osteoarthritis of the hip-joints there would have been much debate on the part to be played in treatment by arthrodesis. It is true that arthrodesis of the joint in which arthritis is most advanced could be supported on the grounds that if one hip is strong and painless the other can be protected. But the alternative claims of arthroplasty of one or both joints by fascial interposition, insertion of a vitallium cup, or excision of the head and neck of the femur, must be weighed carefully when the problem is that of two painful stiff hips. All arthroplasties in the table below were performed for bilateral osteoarthritis.

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Acetabuloplasty	2		

But the discussion is limited to unilateral osteoarthritis of the hip-joint and in these circumstances I suggest that all doubt is removed. A patient with one hip-joint soundly ankylosed in the optimum position, who in every other respect is normal, has so slight a disability that he passes as a normal individual. He has no pain; he has no appreciable limp; he can walk ten or fifteen miles with ease; he can run and jump; he can play games and climb mountains; a man can go back to strenuous labour; a woman can do household duties; she can climb ladders and scrub floors. One patient with an arthrodosed hip-joint is a plate-layer on the railway; he walks 10 miles every day of his life; another is a railway porter; one drives a two-seater car hundreds of miles a week; another used to ski every winter; a lady of 60 went tobogganing within eight months of arthrodesis; her only complaint was that she found it difficult to balance near a precipice! Are these results to be compared with those of arthroplasty? A patient with a vitallium cup may demonstrate free movement when lying on a couch, but can he jump from a five-barred gate? Would he dare to do so? In considering the results of excision of the head and neck of the femur we have heard that most patients rely on walking sticks but some learn to discard their surgical appliances. Walking sticks? Appliances? The patient with a sound arthrodesis would be insulted by the offer of a stick; it would never occur to him to use an appliance. The functional result is so excellent that no arthroplasty, pseudarthrosis or bifurcation osteotomy is to be compared with it.

Disadvantages of arthrodesis of the hip-joint.—(1) *Severity of operation:* The operation is one of some magnitude; it takes at least two hours to perform both stages and apply a plaster spica. One early case in this series died of post-operative shock. But that was ten years ago; it was before I introduced the two-stage operation; it was before blood and plasma transfusions were readily available; it was in the days when even a single pint of blood was given only after the emergency had arisen. During the last few years we have learned to control shock. A plasma drip is started at the beginning of the operation and a ten-minute pulse and blood-pressure chart is kept; by suitable control of the rate of drip it is possible to prevent any semblance of shock. In patients of 30 to 35 years whose arthritis is due to traumatic dislocation or congenital subluxation both stages can be performed in one operation. Even in patients aged 55 to 75 with a two-stage operation there is no greater risk than with any major procedure. Among 70 patients in this series whose hip-joint was arthrodosed for degenerative osteoarthritis the youngest was 40 years and the oldest was 74. The average age was 46.1 years; one died on the tenth day from paralytic ileus; in no other patient in the series of over 300 operations did the question of operative mortality arise.

(2) *A stiff hip is not ideal:* When the procedure is described as "a stiffening operation" the patient may well reflect "My hip is stiff now; whatever will it be like after a stiffening operation?" But the fact is that arthrodesis does not make the joint any stiffer than it becomes without treatment. Moreover, so far as the patient is concerned the hip is not stiff; by virtue of pelvic movement there appears to be 40 or 50 degrees of flexion movement and at least 30 or 40 degrees of adduction-abduction movement. To describe the procedure as "a stiffening operation" is to convey a false impression. If the surgeon actually demonstrates the ultimate range of movement patients do not take exception, particularly since the operation is seldom suggested except for a joint which is already stiff.

(3) *The knee-joint is stiffened*: It is true that ten weeks' immobilization in a plaster spica causes temporary stiffness of the knee-joint; but if the patient is determined and the surgeon is stimulating and enthusiastic there is little difficulty in regaining full movement of the knee-joint by regular active exercise.

(4) *Arthrodesis of the hip-joint causes pain in the back*: This observation is often made but it is untrue. Movement of the lumbosacral joint does not cause pain; it is strain of the joint which causes pain. A hip-joint which is unsoundly ankylosed with flexion-adduction deformity causes compensatory lordosis and scoliosis, and therefore low back pain. But if the joint is soundly ankylosed in the neutral position, so that there is neither protective muscle spasm nor deformity, there is no low back pain. Many patients with untreated osteoarthritis of the hip-joint have pain in the back; some report that the pain is relieved by the operation; none reports that it is aggravated. Even senile change in the intervertebral joints with lipping of vertebral bodies does not contra-indicate arthrodesis. Such changes were present in many patients in this series without giving rise to low back pain.

SUMMARY

In recording 326 operations for arthritis of the hip-joint, including 135 cases of nail arthrodesis for osteoarthritis, it is submitted that the indications are as follows:

(1) Early osteoarthritis of the hip, with 90 degrees or more movement, and ability to walk two or three miles—conservative treatment by electrotherapy, massage, muscle development and the protection of a flannel spica bandage.

(2) Bilateral osteoarthritis of the hip with severe pain, restriction of movement to 30 or 40 degrees, and inability to walk more than about a mile—arthroplasty of one or both hips, or arthrodesis of one and arthroplasty of the other.

(3) Unilateral osteoarthritis of the hip-joint with severe pain, restriction of movement to 30 or 40 degrees, and inability to walk more than about a mile—nail arthrodesis of the arthritic hip.

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Mr. Bryan McFarland discussed the value of the oblique displacement osteotomy for unilateral osteoarthritis of the hip. He described its efficacy for relief of pain and correction of deformity, and its suitability for elderly patients. He illustrated its application in a case of protrusio acetabuli. He stressed the importance of ensuring complete division of the bone so as to obtain adequate displacement, and described a method of fixation without using a plaster of Paris spica.

He showed a film by Professor McMurray illustrating the operation and some results.

Mr. T. T. Stamm: *Arthroplasty*.—This is not usually regarded as a method of choice for unilateral arthritis of the hip. The uncertainty of the results when compared with such measures as arthrodesis or osteotomy has almost entirely limited its field of usefulness to cases of bilateral arthritis. If it were possible to devise the means whereby a stable and painless new joint could be produced with reasonable certainty, the method might take its place beside others even in the treatment of unilateral arthritis. The term arthroplasty is generally taken to refer to some operative procedure whereby the essential features of a new diarthrodial joint are fashioned. In practice, however, it is only possible to construct the skeletal elements of the new joint at operation. It is not possible to make new bearing surfaces, capsule or synovial membrane. These can only be developed subsequently by controlling the organization of the blood-clot lying between and around the new bone ends.

The whole scheme of treatment which ultimately results in the formation of a new diarthrodial joint consists of a preliminary operation, for which the term arthroplasty is used, though often it may be little more than an arthrolisis, followed by a carefully controlled plan of after-treatment. We have no suitable term with which to differentiate between the preliminary operation itself and the whole scheme of treatment which includes the operation, and I would like to suggest that the latter might well be referred to as arthropoiesis, meaning a method of treatment consisting of a preliminary operation, which may be an arthroplasty, arthrolisis or simple excision, and followed by after-treatment resulting in the formation of a new diarthrodial joint.

In most attempts at making a new joint at the hip an endeavour has been made to reproduce as closely as possible the mechanics of the normal hip, and I

believe that this, together with an over-emphasis on the operative rather than the post-operative side of treatment, have been the main causes of failure.

The problem to be considered is twofold: first, the mechanical design of the skeletal elements of the new joint, which will be fashioned at operation, and, second, the plan of post-operative treatment, whereby the other structures of the new joint, synovial membrane, articular surfaces and capsule, will be developed.

Any operation for arthroplasty must entail the removal of bone. In the case of the hip, when sufficient bone has been removed to permit a useful range of movement, it is found that there is insufficient raw material left out of which a satisfactory new joint can be made. It is, therefore, difficult to reproduce the essential mechanics of the joint, and almost impossible to provide a sufficiently large femoral articular surface to bear the weight of the body.

There are only two ways out of this difficulty: (1) To import new raw material as in the "cup" arthroplasty; or (2) not to attempt to reproduce the normal hip, but to design an entirely new joint of the simplest possible type with the raw material available.

Any such new joint should be of the simple hinge or ball and socket type; the axis of movement should be horizontal, in order to avoid shearing strains; the articular surfaces should be as large as possible; and finally, the abductor mechanism should be preserved.

The fact that a freely movable and painless false joint can regularly be obtained by a simple excision of the head and neck of the femur was taken as a starting point. It was argued that if this was combined with an osteotomy of the Shantz type, reasonable stability might also be achieved.

In practice it was found that this combined procedure did give a stable and movable hip, though the mobility was considerably less than with a simple excision. The movements possible, however, were not in the plane of flexion and extension, but in the plane of the side wall of the pelvis.

The next step, therefore, was to bring the axis of the new joint down to the horizontal. This was accomplished by increasing the angle of abduction at the site of osteotomy until the shaft made a right angle with the line joining the greater and lesser trochanters. At the same time a horizontal proximal articular surface was made by leaving the upper part of the head and neck of the femur to form a projecting shelf. This, of course, can only be done where bony ankylosis is present, unless a preliminary arthrodesis has been performed.

The result was a stable and freely movable joint which fulfilled all the theoretical requirements. The joint has a horizontal axis, a large weight-bearing surface and the abductor mechanism has been preserved.

It had, however, two disadvantages. It required two operations, or three if a preliminary arthrodesis had to be done. An attempt was made to combine the two operations in one by plating the osteotomy but this proved to be too formidable a proceeding for routine use. Also it was difficult to prevent the femur becoming displaced laterally during subsequent treatment.

It has now been found that much the same effect can be achieved in a one-stage operation by modifying it. The joint which results still fulfils the criteria laid down, and incidentally by using a lateral approach and turning up the great trochanter, the operation itself is rendered comparatively simple. The trochanter is reattached to the shaft at the end of the operation by one or two screws.

For after-treatment for arthroplasty see *Proc. R. Soc. Med.*, 1942, 35, 221.

Mr. Kenneth H. Pridie: *Vitallium cup arthroplasty.*—During the last four years I have performed 121 operations for arthritis of the hip of which 45 were osteotomy operations. I have chosen vitallium cup arthroplasty in 23% of my series of cases of arthritis of the hip-joint. The factors to be determined are: (a) Is the patient relieved of pain? (b) Is useful movement obtained? (c) How long will this arthroplasty last? (d) On what type of case should this operation be performed? (e) Contra-indications. (f) Complications.

The radiographs of my cases show that the cause of the arthritis has been due to two factors: (1) *Shallow hip or congenital hip dysplasia* (8 cases, 5 of them showing the second factor, aseptic necrosis, locally). (2) *Aseptic necrosis of the head of the femur* (10 cases).

In reviewing my cases I have noticed that in nearly every one there is a vascular calamity in the region of the head of the femur, causing a local or general avascular necrosis of the head. There have been various causes to bring about this condition and it was first brought to my notice by a remarkable case. The patient was a caisson worker who developed this condition as a result of too rapid decompression. Bubbles of nitrogen were liberated in the fat at the upper end of the femur and this ploughed up the region causing damage to the vessels supplying the head. This was followed by a

collapse and break up of both femoral heads. A more massive necrosis may follow a fractured neck of femur that has been pinned, or after a traumatic dislocation.

Cases of idiopathic osteoarthritis occurring suddenly are often due to a similar condition, probably caused by hæmorrhage following trauma.

There were only two cases among these 28 hips that did not show a local avascular necrosis and they had an infective arthritis. Shallow hips seem predisposed to this condition and all these cases showed it very clearly. Pure primary osteoarthritis must be rare in the hip—I believe that it often follows a vascular lesion.

Operative findings.—Few of the cases have a front to the acetabulum. Where there is mushrooming of the head and much bone proliferation with sessile osteophytes there is generally marked thickening, hyperæmia, and polyposis of the synovial membrane. Where hips are fixed the capsule is extremely thin, resembling tissue paper. Large cystic spaces are found in the head of the femur and areas of aseptic necrosis in the upper quadrant of the head. The acetabulum is generally in better condition than the head.

Instruments.—Special instruments have been designed to cut the head to the correct shape. A special acetabular reamer is used which self-cleans. An acetabular cutter is used for shallow hips.

Complications.—(1) Hæmatoma; sepsis—mild 2 cases, severe 2 cases—cup had to be removed. Preventive measure: Drain top and bottom of the wound. Treatment: For mild sepsis open up the wound; for severe sepsis remove cup and leave wound open. Sepsis should be prevented in future by the use of penicillin. (2) Formation of bone round the cup limiting movement. (3) Adduction—? osteotomy later. (4) Cup eating into acetabulum. This may occur in cases where there is marked decalcification—spondylitis ankylopoietica. (5) Absorption of neck and cup eats into digital fossa and base of neck, losing gluteal leverage and causing pain.

Types of cases.—The operation has been performed three times for spondylitis ankylopoietica but each case has been a failure. The immediate result has been encouraging but on late follow-up the hip loses its range of movement. The cups tend to eat their way through the acetabulum and for this type of case if both hips are active (acute and very painful) I advise a blind arthrodesis by a Watson-Jones pin so that the hips ankylose in good position. The patient has the advantage of remaining ambulatory during the period it would have taken for his hips to fuse.

If seen in the stage of ankylosis removal of the head and neck of femur gives a greater range of movement than a cup arthroplasty. Three cup arthroplasties have been performed for aseptic necrosis following fractured neck of femur but the results were poor. After removal of the dead portion of the head there is not enough bone left to keep the cup off the base of the neck which is tender. In one of the cases the cup pressed on the region of the neck and digital fossa causing pain and this result has not been good. The other two cases became infected.

These cases are extremely vascular owing to nature's effort to give a new blood supply via adhesions of vascular capsule to the neck. The bleeding is very severe and uncontrollable and all these cases have developed hæmatomata. The rest of the series have not been troubled with this complication.

The operation has also been performed for protrusio acetabuli affecting both hips. The result, however, was a failure as the cup was lost in the deep acetabulum and no movement was obtained.

RESULTS

Relief of pain.—This is dramatic—most patients appear to be delighted and do not mind the limp and slight disability. *Function.*—During the first year this is disappointing and most patients walk with one or two sticks. There is a great improvement in the second year and by the third year the range of movement has increased considerably. *Advantages over other methods.*—(1) The patient is able to start walking in five weeks. (2) The patient can sit better than a similar case after an arthrodesis operation. This is much appreciated by the aged and by women.

Indications for cup arthroplasty.—(1) The chief indication for cup arthroplasty is the presence of severe pain due to bilateral arthritis of hips. The patients on whom I performed the operation for this reason were all extremely crippled with severe pain. They were completely incapacitated and nothing could have made them worse. All these cases have been much improved and are delighted with the result. Although one of them walks with two crutches he is free of pain and is back at work. He is a failure as far as the arthroplasty is concerned but the operation has given him great relief.

(2) Severe pain in one hip in an old person with osteoarthritis of the spine as well.

(3) Shallow hip which tends to dislocate and produce arthritis.

CONCLUSIONS

This is not an operation for the young, nor for the early case of arthritis, nor for the case of aseptic necrosis of the head of the femur following an intracapsular fracture. It is an operation to relieve pain in a really severe case of arthritis in a person over 50, particularly in those unfortunate cases with severe bilateral arthritis. This operation should be done in special hospitals with full equipment and complete set-up.

Section for the Study of Disease in Children

President—HELEN M. M. MACKAY, M.D., F.R.C.P.

[November 24, 1944]

DISCUSSION ON SUBDURAL HÆMATOMA IN INFANCY

Commander R. Cannon Eley, U.S.N.R., M.C. : Introduction.—The occurrence of subdural hæmatomas in infancy is not a new clinical or pathological entity, but instead a condition which has been recognized during the past few years with increasing frequency. This recognition has been made possible by a better understanding of clinical manifestations and by improved diagnostic procedures.

This statement that subdural hæmatoma is not a new clinical entity is based on evidence accumulated by encephalography and ventriculography, for surely such pneumo-encephalograms as we have seen in the past could hardly have resulted from any other cause. Autopsy studies and reports lend further support to this statement. Unfortunately the condition is still referred to loosely as pachymeningitis hæmorrhagica interna, and this leads to further confusion as the two disturbances are entirely different.

By subdural hæmatoma, we simply mean an accumulation or "pocket" of blood between the dura and the arachnoid membranes. The usual anatomical site is the fronto-parietal area. The distribution may be unilateral, but it is often bilateral.

Symptomatology.—One is required to be constantly aware of its possibility, and to suspect it whenever a certain group of symptoms or signs is present, or whenever a diagnosis cannot readily be established. The latter statement may seem rather abstruse, but it is true, for the clinical manifestations are protean in nature; they vary a great deal and are not always pathognomonic.

Formerly the presence of convulsions, accompanied by a gradual enlargement of the head, was considered the cardinal sign and symptom. However, it is now recognized that these are often *late manifestations*, which have been preceded by such *symptoms* as: Refusal to nurse properly, or at all; failure to gain in a normal manner; unusual lethargy, even stupor, or, conversely, hyper-irritability ("crying baby", "tense", "nervous baby", &c.); vomiting without adequate explanation; convulsions: localized, generalized or *pétit mal*.

Associated with these symptoms, the following *signs* may be present: Exaggerated or hyperactive reflexes; separated sutures and tense or bulging fontanelle; tonic neck reflexes; generalized muscular hypertonicity; hemiplegia, diplegia or monoplegia; downward displacement of eyes (pupil lower, &c.); petechial or gross hæmorrhages into retina; irregular temperatures (elevated or subnormal); optic atrophy (rare); "cracked-pot" sound; enlargement of the head.

Establishment of diagnosis of subdural hæmatoma.—Now let us assume that from the history and the physical examination we suspect the presence of a subdural hæmorrhage. The diagnosis can be established by: (1) *Subdural tap*: (a) Nature, i.e. colour of fluid. This will depend upon the duration of the presence of blood or the products of hæmo-

lysis; (b) high protein content of the fluid removed. (2) *Lumbar puncture*: If the cerebrospinal fluid is clear, as it often is, only one lumbar puncture is indicated. (3) *Röntgenological evidence*, as demonstrated by encephalography or ventriculography.

Differential diagnosis.—The presence of bloody subdural fluid establishes the presence of a subdural hæmatoma only. It does not establish the *ætiology* of the hæmatoma. To assume that the hæmatoma is necessarily due to trauma and to introduce operative procedures is a poor policy which, if followed, may lead to disaster. One is justified in assuming that the hæmatoma is due to trauma only after the exclusion of certain other disturbances which are conducive to intracranial hæmorrhage such as: (1) Purpura—idiopathic or symptomatic. (2) Leukemia. (3) Spontaneous meningeal hæmorrhage. (4) Hæmophilia. (5) Scurvy. (6) Lues. (7) Infection, &c.

Each of the above disturbances may be excluded by the history, physical examination and appropriate laboratory procedures.

Ætiology.—This brings us to the discussion of the *ætiology*. Several theories and hypotheses have been advanced, but after each has received due consideration, we find that trauma occupies the first position. Trauma may be (i) *pre-natal*, or (ii) *post-natal*. When the moving head strikes an immovable body, be it the human pelvis or some object such as a floor or a wall, a physical derangement of the intracranial structures occurs, and this may cause a rupture of blood-vessels leading from the superior aspect of the cerebral cortex to the longitudinal sinus. Hence the explanation of the frequency of bilateral lesions.

Apart from trauma, other factors which may be of importance are: (1) *Age*.—The largest number of cases seen at the Children's Hospital, Boston, occurred during the first six months of life, especially during the four to six months' period.

(2) *Sex*.—60% of the patients have been males.

(3) *Infection*.—Often present, but not of primary significance.

(4) *Scurvy*.—Ingalls (Ingalls, T. H., 1936, *New Engl. J. Med.*, 215, 1279) made a study of a group of patients with subdural hæmatoma and demonstrated that many of them had some degree of vitamin-C deficiency. This, of course, made it possible for even slight trauma to precipitate a hæmorrhage. However, I feel that one must conclude that this is not the cause *per se*, but simply an existing state which enhances the possibility of hæmorrhage following trauma to the head.

(5) *Malnutrition*.—Sherwood (Sherwood, D., 1930, *Amer. Journ. Dis. Child.*, 39, 980) in 1929 reported on a series of 11 cases of subdural hæmatoma and indicated the frequency of malnutrition among these infants and the poor economic status of the families. Here again we meet with a contributory factor rather than the cause. Scurvy, as well as the other deficiency diseases, are often associated with malnutrition.

In summary, then, we may say that although the presence of other conditions may indicate the development of a subdural hæmatoma, yet trauma is the chief precipitating factor.

Pathology.—A discussion of the treatment of subdural hæmatoma presupposes that one is possessed of a knowledge of the underlying pathology, for proper treatment, whether medical or surgical, is based upon pathological changes. These are briefly reviewed:

Subsequent to trauma, hæmorrhage develops between the dura and the arachnoid membranes. As the blood-vessels in the dura are largely on its outer surface and quite minute, the bleeding usually arises from the pial vessels which extend from the cortex to the lacunar spaces of the superior longitudinal sinus, and therefore are more subject to stretching and rupture by trauma.

The resulting clot usually extends from the posterior parietal area forward and over the frontal lobes. Since the brain experiences the trauma in its entirety, the bleeding is often bilateral. Between the *second and third week* following clot formation, vascularization begins and there is an outgrowth of fibroblasts from the inner surface of the dura which gradually encapsulates the entire clot. At first the membrane is closely adherent to the inner aspect of the dura, but as vascularization continues, it becomes thicker and finally forms a structure separate from the dura. The gross and microscopic pathologic characteristics of this process have been sufficiently studied and discussed in the literature (Leary, T., 1934, *J. Amer. med. Ass.*, 103, 897) and are familiar to those interested in this subject. They need not be considered in detail at this time.

Hæmolysis of the sac contents naturally follows encapsulation, and the resulting fluid has a very high protein content. The high protein concentration of the sac contents exerts an osmotic effect, so with time more fluid may be drawn into the sac. In other words, the sac may and does continue to enlarge, even though further bleeding does

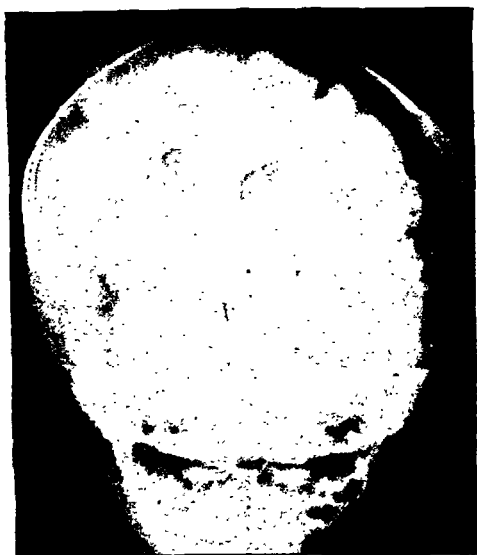


FIG. 1 (Case I).—Subdural hæmatoma. Air encephalogram showing widening and depression of sulci, especially in left frontal area; asymmetry of ventricles.

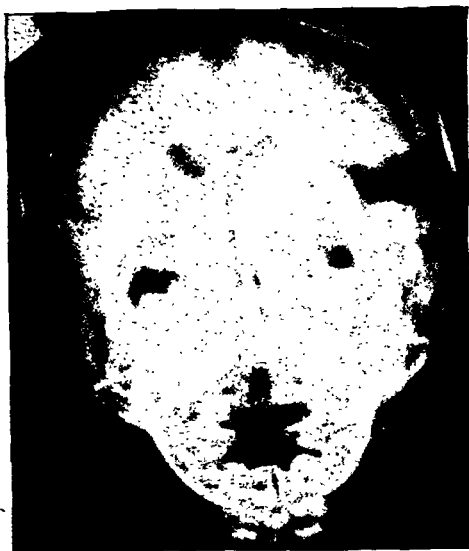


FIG. 3 (Case III).—? Porencephalic cyst. ? subdural hæmatoma. Air encephalogram showing large air-containing space over the cerebral hemisphere.



FIG. 2 (Case II).—Cerebral agenesis. Air encephalogram showing large collection of air in the frontal region.

Illustrating Dr. Janet Gimson's cases (see next page).

the cause. At one might expect the outer membrane, but the one next to the dura is less permeable, less elastic and more durable than the inner one, which is of a thin, filmy nature and well-permeable. From this brief description, it does not require much speculation to appreciate the effect of the continuous pressure exerted by the arrested fluid against the brain, and the progressive, irreparable damage which must follow. Pressure by the "top" and compression by the membrane produce ischaemia and thrombosis followed by atrophy.

The Bureau of Medicine and Surgery, U.S. Navy, does not necessarily undertake to endorse views or opinions which may be expressed in this paper.

Dr. Janet D. Gimson: Three cases are briefly reported, all of which have recently been in the Hospital for Sick Children, Great Ormond Street, W.C.1, under the care of Dr. Donald Peterson. Influenced by the paper of Ingraham and Mason, *J. Pediatr.* 1931, 44, 1-37, and by discussions with our American visitors, we felt bound to look actively for cases of subdural hæmatoma. These three show to some extent the diversity of symptoms from which such patients may suffer. They also illustrate the fact that one cannot diagnose the condition without looking for it and without carrying out the diagnostic procedures as indicated by Ingraham and Mason.

(1) *Subdural*.—This baby presented at 11 weeks old having had multitudinous convulsions for the previous six days. First child, full term, birth-weight 7 lb. 4 oz. Forceps delivery, one blade having been applied over the left frontal area where there was a marked depression and asymmetry of the skull. Head circumference $14\frac{1}{2}$ in. In addition to the convulsions the baby had been vomiting periodically during the past three weeks. Expected weight 11 lb. 7 oz. Actual weight 10 lb. (artificially fed). No elevation or depression of temperature.

Special examination.—Lumbar puncture—C.S.F. normal. Optic atrophy bilateral. *Air encephalogram*: Widening and depression of sulci, especially in left frontal area. Asymmetry of ventricles (fig. 1, p. 371). *Subdural tap*: 0.5 c.c. clear fluid from right. Xanthochromic fluid under tension, 5 to 6 c.c. were withdrawn from left. Protein content of this fluid: 200 mg. %.

The subdural tap was repeated in the left frontoparietal suture line at two or three day intervals. After the second tap the fits diminished somewhat in number and intensity. They became countable, 6 to 8 per day. Mr. Harver Jackson was called in and decided to burr-hole and explore. The sixth tap the day before operation produced no fluid. At operation Mr. Jackson found a thin layer of granulations and a membrane which he evacuated as far as possible. The fits are less frequent 2 to 4 per day, but they still continue.

(2) *Cerebral agenesis*.—This baby was sent up on the 6th day of life with the diagnosis of intestinal obstruction. First baby, normal labour, full term, birth-weight 7 lb. 8 oz. The baby had been sleepy over its feeds and had vomited everything. It had passed nothing but meconium. It had lost weight to 6 lb. 12 oz. The first thing on admission of course was the passage of a normal stool but feeding continued to be difficult; he continued with occasional vomits and he would not suck. The shape of the head was peculiar though not asymmetrical; the anterior fontanelle was widely open right down to the nasion. However, in appearance, it was exactly like that of the father.

Examination.—Optic fundi: Bilateral partial optic atrophy. *Air encephalogram*: Large collection of air in the frontal region, no asymmetry of the ventricles (fig. 2). *Subdural tap*: about 0.5 c.c. of normal clear C.S.F. obtained each side.

(3) ? *Porencephalic cyst*; ? *subdural hæmatoma*.—This baby attended at the age of 24 days. First baby, full term, normal labour. He had the classical symptoms of pyloric stenosis, projectile vomiting, constipation and loss of weight. He was so dehydrated that an intravenous transfusion was required to prepare him for Rammstedt's operation. This was performed under a local anæsthetic and a large tumour was found. The normal post-operative progress was not maintained. He was very pale, he continued to regurgitate, his weight remained stationary. Then five days after operation the baby had a generalized convulsion. Two days later he had two more convulsions.

Examination.—Optic fundi: Bilateral atrophy. *Air encephalogram*: Large air-containing space over the cerebral hemisphere (fig. 3). *Subdural tap*: Right 0.2 c.c. of normal C.S.F. Left—clear xanthochromic fluid 4 to 5 c.c. with a protein content of 70 mg. was obtained. Lumbar puncture: C.S.F. normal.

There is no difficulty in performing pneumo-encephalograms and subdural taps. These investigations are of assistance in the diagnosis of subdural hæmatoma, but the treatment must be left to the surgeon.

[January 26, 1945]

DISCUSSION ON THE SCHOOL MEDICAL SERVICE—PRESENT AND FUTURE

Dr. John D. Kershaw: We have now a self-contained school medical service which has three main objectives—the detection and cure, at the earliest possible stage, of defects, diseases and tendencies to defect and disease, the prevention of defects and disease by such means as the development of school and personal hygiene, health education and the anticipation of malnutrition by the provision of milk and meals in school, and, perhaps most important of all, constructive work—to enable the child to realize his full potentialities for health.

We seek these ends by a variety of means. Our basis is periodical medical examination—I deliberately avoid the term “routine medical inspection”—coupled with surveillance of a less formal kind between the periodical examinations and the provision of inspection clinics to which children may be referred by parents or teachers if any defect is suspected. We provide treatment which falls into three main classes, the treatment of minor ailments, the treatment by specialists of conditions which fall outside the scope of general medical practice and the provision of certain special forms of treatment which are, perhaps, rather of the nature of special education than of active medicine and range from speech therapy through orthoptics and the special education of myopes in “sight-saving classes” to the provision of day and residential special schools. Important by-products of the Service have been research on a considerable scale into nutrition and into many forms of disease and defect—one may mention particularly the study of nose and throat affections and such quasi-orthopædic subjects as posture—and the development of new techniques of treatment such as orthoptics, zinc ionization for otorrhœa and child guidance.

Our task now is to consider the present service critically. Our school medical service, excellent though it may be within its compass, deals with a child who has been an infant and will, later, become a young worker, with an individual whose school life, though important, must not be divided too strictly from his home life, and with a human body which suffers not only from minor ailments but from major ones.

We have already got a partial integration of school medicine with child welfare and the environmental health services in that the local administration of all of them is, in many places, in the hands of the same person, the Medical Officer of Health. This, however, is not universal. Even where it does exist, the health visitors and school nurses may be different persons and the school medical service may be rigidly departmentalized, and we have a considerable number of towns where the town itself is the child welfare authority but the county council is responsible for the school medical service. There is, as yet, no co-ordination worth mentioning between school medicine and industrial medicine as it applies to the adolescent.

Before all else we need to establish a unified child health service which will care for the child continuously from birth to maturity and will be co-ordinated with those other services which are concerned with the child before birth. We might do worse than establish a Ministry of Child Health which would gather together those miscellaneous provisions which are, somewhat arbitrarily, divided between the Ministry of Health, the Ministry of Education and the Home Office, so that centrally, at least, there is neither schism nor interdepartmental jealousy.

At the same time, however, we must not neglect those points which mark out school life as a special part of childhood. We logically regard the family as the basic social unit, but we must not ignore the fact that the school is also a social unit and one of special significance, not only because the child spends more of his waking life in school than in any other place, not only because in the school we have the child in health and in sickness in a controlled environment ready to our hand and need not wait until sickness makes him seek our aid, but because the school is the only place in which we, as a community, are deliberately bringing formative influences to bear on him to prepare him for his later share in the community's life.

Because of these facts and because, also, the child's school days coincide with certain special and important periods of mental and physical development, the school medical service will necessarily have a distinct, though not a separate, place of its own in this new and wider child health service.

We must now consider the isolation of the school medical service from the provision of domiciliary care and from the work of the family doctor generally. Medicine is, at present, a competitive profession, and a patient is a source of income, actual or potential,

not occur. As one might expect, the outer membrane, i.e. the one next to the dura, is less permeable, less elastic and more durable than the inner one, which is of a thin, filmy nature and semi-permeable. From this brief description, it does not require much imagination to appreciate the effect of the continuous pressure exerted by the encysted fluid against the brain, and the progressive, irreparable damage which must follow. Pressure by the "cyst" and constriction by the membrane produce ischemia, and ischæmia is followed by atrophy.

The Bureau of Medicine and Surgery, U.S. Navy, does not necessarily undertake to endorse views or opinions which may be expressed in this paper.

Dr. Janet D. Gimson: Three cases are briefly reported, all of which have recently been in the Hospital for Sick Children, Great Ormond Street, W.C.1, under the care of Dr. Donald Paterson. Stimulated by the paper of Ingraham and Matson (*J. Pediat.*, 1944, 44, 1-37) and by discussions with our American visitors, we felt bound to look actively for cases of subdural hæmatoma. These three show to some extent the diversity of symptoms from which such patients may suffer. They also illustrate the fact that one cannot diagnose the condition without looking for it and without carrying out the diagnostic procedures as indicated by Ingraham and Matson.

(1) *Subdural*.—This baby presented at 11 weeks old having had multitudinous convulsions for the previous six days. First child, full term, birth-weight 7 lb. 4 oz. Forceps delivery, one blade having been applied over the left frontal area where there was a marked depression and asymmetry of the skull. Head circumference 14½ in. In addition to the convulsions the baby had been vomiting periodically during the past three weeks. Expected weight 11 lb. 7 oz. Actual weight 10 lb. (artificially fed). No elevation or depression of temperature.

Special examination.—Lumbar puncture—C.S.F. normal. Optic atrophy bilateral. *Air encephalogram*: Widening and depression of sulci, especially in left frontal area. Asymmetry of ventricles (fig. 1, p. 371). *Subdural tap*: 0.5 c.c. clear fluid from right. Xanthochromic fluid under tension, 5 to 6 c.c. were withdrawn from left. Protein content of this fluid: 200 mg. %.

The subdural tap was repeated in the left frontoparietal suture line at two or three day intervals. After the second tap the fits diminished somewhat in number and intensity. They became countable, 6 to 8 per day. Mr. Harvey Jackson was called in and decided to burr-hole and explore. The sixth tap the day before operation produced no fluid. At operation Mr. Jackson found a thin layer of granulations and a membrane which he evacuated as far as possible. The fits are less frequent 2 to 4 per day, but they still continue.

(2) *Cerebral agenesis*.—This baby was sent up on the 6th day of life with the diagnosis of intestinal obstruction. First baby, normal labour, full term, birth-weight 7 lb. 8 oz. The baby had been sleepy over its feeds and had vomited everything. It had passed nothing but meconium. It had lost weight to 6 lb. 12 oz. The first thing on admission of course was the passage of a normal stool, but feeding continued to be difficult; he continued with occasional vomits and he would not suck. The shape of the head was peculiar though not asymmetrical; the anterior fontanelle was widely open right down to the nasion. However, in appearance, it was exactly like that of the father.

Examination.—Optic fundi: Bilateral partial optic atrophy. *Air encephalogram*: Large collection of air in the frontal region, no asymmetry of the ventricles (fig. 2). *Subdural tap*: about 0.5 c.c. of normal clear C.S.F. obtained each side.

(3) ? *Pörencephalic cyst*; ? *subdural hæmatoma*.—This baby attended at the age of 24 days. First baby, full term, normal labour. He had the classical symptoms of pyloric stenosis, projectile vomiting, constipation and loss of weight. He was so dehydrated that an intravenous transfusion was required to prepare him for Rammstedt's operation. This was performed under a local anæsthetic and a large tumour was found. The normal post-operative progress was not maintained. He was very pale, he continued to regurgitate, his weight remained stationary. Then five days after operation the baby had a generalized convulsion. Two days later he had two more convulsions.

Examination.—Optic fundi: Bilateral atrophy. *Air encephalogram*: Large air-containing space over the cerebral hemisphere (fig. 3). *Subdural tap*: Right 0.2 c.c. of normal C.S.F. Left—clear xanthochromic fluid 4 to 5 c.c. with a protein content of 70 mg. was obtained. Lumbar puncture: C.S.F. normal.

There is no difficulty in performing pneumo-encephalograms and subdural taps. These investigations are of assistance in the diagnosis of subdural hæmatoma, but the treatment must be left to the surgeon.

work of school medicine should offer a full and satisfying career, spiritually and materially, to the right person. I should like to see entering the service men and women who have had some special training in child health and pædiatrics, and whose work would not only consist of periodical medical examinations but would bring them into regular and close contact with the educational system generally. They would visit schools to get to know school, teacher and child, and would, among other things, have duties in connexion with the ancillary services of school medicine—health education, school meals, physical education and school hygiene. They might hold clinical assistantships in hospitals and they would certainly have a place in the health centres on which we expect our future health services to be based.

It is worth while here to say a word in season on the position of the pædiatrician. Pædiatrics and school medicine are not the same, nor yet are they entirely different. They are distinct but complimentary parts of the same whole. I have just suggested that the school medical officer should know something of the sick child as well as the healthy one and I feel that it would be all to the good if every recognized pædiatrician were required to spend, as part of his training for that specialty, a period as a school medical officer.

The school medical service has been built by degrees within the legislative framework of the educational system and has, in the past, met serious difficulties from this very cause. The school dental service has had little or no basis in law—it could, I think, be claimed on legal grounds that every school dental inspection is a technical assault. The parent has never been compelled to present a child for medical inspection—it is only when a child is known or believed to have a defect that examination is compulsory. Technically the provision of treatment for defects has always in the past rested upon the question of whether those defects rendered the child unable to benefit by his education. I believe that the 1944 Education Act will go a long way toward removing the worst of these anomalies, but, by preserving that basic idea that the school medical service is legally an appendage of education, there is a serious danger that it may create new difficulties. A considerable number of local authorities, for instance, will this year lose control of their school medical service to the County Councils, although they will retain their child welfare services, a positive worsening of a serious defect which I mentioned earlier. We are promised that at some later date the child welfare service will "follow" education: it is no remedy for the divorce of school medicine from child welfare to divorce both of them from the environmental health services and it is important that we should do something quickly to ensure that this divorce is not accompanied by too much estrangement.

Before the war, each annual report of the chief medical officer to the Board of Education contained a long and imposing list of researches carried out by school medical officers. It would have been unfortunate if that had not been so; the wealth of material ready to hand was such that to neglect it would have been criminal. I have already mentioned or implied some of the subjects of those researches, but as one who engaged in them I have a first-hand knowledge of their limitations.

Every fact has value, but its own internal value is small compared with that which it derives from being linked with other facts, and it has always struck me as strange that a service which was nominally a national whole made little or no effort to co-ordinate the researches of its various members. I have previously mentioned the need for changing our objective from the attainment of the "normal" to a striving after the optimum and one of the most urgent tasks of the school medical service is to seek to discover what that optimum may be.

To that end we need, and I am encouraged to hope that we may shortly have, a new and closer understanding between the academic worker and the field worker. I hope to see our University Departments and Institutes of Child Health and Social Medicine taking the school medical officer into partnership in this work. Instead of the individual officer being compelled to learn by his own painful mistakes, he will have expert help in the planning of research and technical assistance in such matters as the statistical assessment of his results. The "amateur" researcher is not to be sneered at by the professional: research is a labour of love and even the man whose profession it is must remain an amateur in the best sense of the word. In the schools we have our research material accessible and its full use is a social duty.

Dr. Isobel Wright: Present supervision of the 2-5 year age-group comprises:—

- (1) Periodic home visits by the health visitor who advises on general hygiene, régime, and diet.
- (2) Voluntary attendance at infant welfare centres for medical examination and periodic

to his doctor. In theory and even in practice the school medical service is taking the bread out of the mouth of the family doctor. We cannot expect any satisfactory integration of school medicine and out-of-school medicine until we have a whole-time salaried State medical service.

If we can make some clear and intelligent distinction between those forms of treatment which can most properly be assigned to the family doctor and those which are plainly the business of the school medical service itself we can make the way clear for at least some measure of co-operation even under present conditions.

Domiciliary medical care is, clearly, the family doctor's province. Of the work which the school clinics do at present I would suggest that a great part of the minor ailment treatment could also be done by the family doctor. What the family doctor cannot do is work which requires facilities which are outside his normal range of equipment. It is obviously better, for example, that the school medical service should have a large light therapy unit for school children than that every doctor in town should have a small one. The same consideration will apply where the facilities consist not so much of equipment as of the work of medical auxiliaries, and its force will be increased by the fact that some medical auxiliaries—the speech therapist, the orthoptist and the expert in remedial exercises, for example—do work which is partly medical and partly educational and will function to the best advantage if their activities are directly linked with the schools through the school medical service.

Treatment which requires the services of a consulting physician or surgeon is, at present, reasonably adequately provided by the employment in the service of whole-time or part-time consultants, a system which works well and need not be interfered with. It is supplemented, in many instances, by the carrying out of semi-specialist work by school medical officers who have had special experience in some particular branch and who gain enormously from having such opportunity to practise a clinical specialty. Adequate, generally, are the provisions made for such treatment as can only be carried out in hospitals and there is no dispute as to their proper place, while equally beyond dispute is the fact that those medical services which are provided through special schools and classes are undoubtedly a logical part of the school medical service.

Is it too much to hope that if this "encroachment" bogey can be finally laid we shall see school medical records made available to the family doctor and the family doctor keeping the school medical officer posted with knowledge of the child's out-of-school illnesses, so that from this pooling of information we shall have complete and continuous knowledge of every child?

At this stage it is pertinent to consider the suggestion which has been recently made that general practitioners should carry out school medical inspection on a part-time basis. The suggestion has been made on grounds of expediency; we need more frequent periodical examinations of school children but lack the staff. We are told, however, that there is a shortage of general practitioners and I certainly know of none who confess themselves underworked. Further, the irregular urgencies and emergencies of general practice do not adapt themselves to regular sessional employment in part-time work, nor will the competitive nature of private practice readily accept a system by which one general practitioner sees the patients of others in the schools.

My objection to the suggestion is, however, based principally on other considerations. School medical inspection may have been originally introduced for the rapid detection of incipient defects and diseases, but the good school medical officer sees far more in it than that. We in the service have recently been discussing the scope of the periodical examination and, after drawing up a lengthy schedule of possible defects which should be looked for, we were compelled to acknowledge that in all our work there was something else which we could not define better than to suggest that it was of the nature of a complete audit of the child, in consultation with both the parent and the teacher; the drawing up of a mental and physical balance-sheet and the making of constructive suggestions not only for the remedying of defects but for the bringing out of positive potentialities. I am convinced that a doctor who never enters the school except for his occasional inspection sessions and who never sees the child outside school unless he is actually ill can no more make such an audit accurately and well than a man can deduce from the "still" pictures outside a cinema the whole of the film which is showing inside. It is better to retain for the present our infrequent inspections than to debase them into something to which the epithet "routine" is the only one which can be applied.

The backbone of the school medical service must continue to be the full-time officer, but we must acknowledge and remedy the faults of our present system of staffing.

Although the future administrator should still begin with clinical work, the clinical

JOINT DISCUSSION No. 1

Section of Surgery with Section of Proctology

Chairman—SIR JAMES WALTON, K.C.V.O., M.S.

[President of the Section of Surgery]

[February 7, 1945]

DISCUSSION ON THE PATHOLOGY AND TREATMENT OF
CARCINOMA OF THE COLON

Mr. Rodney Maingot: During recent years there have been many noteworthy advances in the management of patients suffering from carcinoma of the colon. Not only is the eradication of the lesion now possible in the majority of such cases, but the operation is associated with a low death-rate.

When we compare the prognosis of cancer in the colon with that occurring in other parts of the body, it is obvious that the colon represents one of the most favourable sites for cure. Before the present war the resection-rate was 50 to 60%; to-day it is about 80%, even excluding the excellent operability-rates of R. Cattell (1943) 84%, A. W. Allen (1943) 91%, and O. Wangenstein (1943) 93%.

The inoperable case is fast becoming a rarity. Until about 1938 radical resection of the colon for cancer gave in the hands of most surgeons a mortality of approximately 20%. Thus in a series of 3,000 cases collected by Ochsner and DeBakey (1939) there were 422 deaths—14%. During the last five or six years, however, there has been a most gratifying and dramatic fall in the operative mortality which coincides with a period in which, owing to improved pre- and post-operative measures and safer anaesthesia, surgeons have shown greatly increased courage, tenacity of purpose and skill in the eradication of malignant processes of the bowel. There are indeed now few cancerous lesions within the abdomen which the expert and determined surgeon cannot extirpate. He has learned that resection affords the maximum degree of palliation; that multiple resections may on occasion yield a brilliant cure; and that, even in the presence of hepatic metastases, if the growth is capable of removal, this should be unhesitatingly performed.

At the Mayo Clinic between 1907 and 1938 there were 8,000 cases of excision of the colon for carcinoma with an operative mortality of 18.5%. In 1942, however, there were 879 patients who were subjected to resection and the death-rate was only 5.1%. A standard of excellence has been set for us by Gordon-Taylor who up to April 1941 performed 138 exteriorization-resection operations for cases of carcinoma of the colon with only seven deaths—a mortality of about 5%.

The life-expectancy following adequate removal of carcinoma of the colon is relatively good, and many clinics can claim 40 to 50% of five-year cures. Cattell (1944) states that 55% of his patients with carcinoma of the colon who had undergone resection showed no evidence of recurrence for five to nine years. Dixon's figures (1944) are even better—five-year cures: right colon 72%; descending colon 63%; and sigmoid colon 44%. His findings support the truth that the prospect of cure following excision of the colon decreases from the caecum through the more distal segments.

Among the many factors responsible for the encouraging advances in this field I would mention: (1) Earlier recognition of carcinoma of the colon due to improved radiological methods; (2) a better understanding among surgeons of the importance and the means of maintaining fluid, vitamin C, electrolyte, and protein balance before and after operation; (3) the treatment of shock by plasma and whole-blood transfusions; (4) the universal acceptance of the principle that a primary resection of the colon should *never* be performed in the presence of acute or subacute obstruction; (5) the measures now adopted in the immediate pre- and post-operative phases for ensuring adequate decompression of the intestine by means of an indwelling intestinal tube or Miller-Abbott tube; (6) the control of infection by means of sulphonamide drugs and penicillin, and the mitigation of bacterial activity within the bowel by the administration of sulphasuxidine in adequate dosage before and after operation; (7) improved anaesthetic methods which permit the surgeon to be more deliberate and painstaking in his operative procedures; (8) the more general utilization of stage operations for resectable growths of the large bowel.

weighing; it has been estimated that some 50% of the 2-5 year age-group attend. Facilities for dental and ophthalmic treatment are usually available; minor ailments can be dealt with by reference to the school clinic if necessary; and provision is made by many local authorities for orthopaedic treatment, massage and remedial exercises, ultraviolet light treatment, and consultations at a child guidance clinic. It is common to have special sessions for the examination of children over 1 year of age; appointments are made so that adequate time can be given for a full discussion with the mother as to the child's progress and well-being.

(3) Day nurseries: these are mainly at the present time for the children of mothers who are engaged on war work, and babies and children up to 5 years of age are admitted. The Ministry of Health stipulates that only two children may be admitted from one family; where there are other pre-school children and the mother wishes to go out to work, this may result in the use of a daily minder—often a very unsatisfactory arrangement if supervision is inadequate. The nurseries are staffed by a matron, nursery nurses, a nursery teacher, and domestic workers. Regular visits are made by a medical officer. Diphtheria immunization is urged if this has not been effected. It would be interesting to know the consensus of opinion of the meeting as to the efficacy of preventive inoculation against whooping-cough.

(4) Nursery classes are available at some of the ordinary elementary schools. A wartime difficulty is the finding of adequate accommodation and suitably trained staff, and sometimes the under-fives have to be taught with the 5-year school entrants: There may be facilities for the use of a play centre—where the children can stay on the premises after school hours until the mother returns from work. Tea is provided, and there are games and play equipment with general supervision by members of the teaching staff.

The new legislation decrees that the provision of nursery schools is a duty imposed on local authorities where the need arises. Day nurseries may cease to exist, though many of us hope that some will be retained, so that the busy mother may have occasionally a few hours' relief from the constant supervision of her family, or for emergency use if the mother is away and the child needs care during the daytime. More useful still are residential nurseries to which the child can be admitted during the time of the mother's confinement, or during acute illness or sudden emergency in the home; also to cope with the upbringing of the younger members of problem families. I should like to interpolate an especial plea for social planning to try to solve the difficulty of what we term the "bad" families.

It remains to be seen to what extent there will be a demand for nursery classes and nursery schools. Opinions are divided as to the wisdom of taking the child from its home environment at as early an age as 2; and doubts have been expressed as to the advisability of grouping together at an age when the morbidity rate is high.

Ideally the nursery school should be one-storied, of the open-air verandah type, in the vicinity of the ordinary school premises but with separate playground and offices.

In view of the high morbidity rate of the 2-5 year age-group adequate supervision from the health point of view is vitally important. It has been suggested that the local health visitor should inspect the children daily, and that the medical officer should attend at least once a week. Arrangements should be made for the transference of the child's record cards from the welfare centre or from the health visitor to the nursery school. To facilitate statistical analysis it would be very helpful if uniform methods of classification and tabulation of records were established throughout the country. Regular height and weight measurements should be made, possibly at the beginning and end of each term. A complete physical examination should be effected at least every six months. Opportunity is afforded for investigation and research in the study of the physical and mental development of these groups of children who are under similar environmental influence for a considerable part of each day. It is hoped that medical students and post-graduates will be interested to attend periodically to observe the normal progress and development of the children, and to learn how to recognize and deal with minor deviations from normal physical and mental health. An extension of parents' associations is envisaged, with meetings at which health propaganda and health problems of the young child can be discussed with medical officer and staff.

As in the ordinary elementary schools, milk and dinners will be provided. We must insist that the milk is efficiently pasteurized, and delivered in small individual bottles rather than in bulk supply. The planning for the provision of meals should be supervised by a dietetic expert in co-operation with the medical staff, and I would like to see compulsory periodic medical examination of canteen and kitchen staff in addition to the usual regular inspections of the actual premises.

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many surgeons in various clinics throughout the world. This operation, too, remained unchallenged by any serious criticism until some thirteen years ago, when the resurrected and improved exteriorization-resection procedures of Bryant, Bloch, Paul and Mikulicz came to be applied to the right segment of the large bowel. This operation was advocated by Lahey in 1932 and has given such excellent results that in my opinion it is without doubt the procedure of choice for tumours of the proximal colon.

The main criticisms which have so far been directed against the Paul-Mikulicz operation for carcinoma of the right colon are:

The excision of the colon with its gland-bearing mesentery effected by this method is neither so liberal nor so radical as that afforded by resection and sutured anastomosis.

For a period of at least six weeks the bulk of the eroding ileal contents is discharged on to the abdominal wall, which, in spite of assiduous attention, may become inflamed and excoriated over a wide area.

Convalescence is unduly protracted and another operation which may be difficult and unsuccessful is required to close the double-barrelled colostomy.

The operative mortality is not materially reduced by the adoption of this method.

I think it can in all fairness be stated that the modernized and improved Paul-Mikulicz operation as performed to-day is not only applicable to malignant lesions from the last loop of the ileum to the lower portion of the sigmoid colon, but can be carried out in such a manner that it is in every respect as thorough and as radical as primary resection and anastomosis.

The secret of securing a wide excision of mesentery of the colon lies in the adoption of the ingenious method of mobilization of the colon to which Kocher, W. J. Mayo, Moynihan and Grey Turner called attention many years ago.

Experience would lead me to emphasize that the exteriorization-resection operation, when performed on the proximal colon, ensures just as wide an excision of the ileum, ascending colon and part of the transverse colon, together with the involved or potentially involved mesentery, as primary resection and anastomosis, nor am I aware of any factors which would in any given case prohibit a liberal mobilization or excision of the parts concerned in the operation. The resulting single stoma, which remains in the abdominal wound after the long 5-inch spur between the two limbs of bowel has been effectively cut through with an enterotome, can be successfully closed in every instance with little or no risk by a simple extraperitoneal procedure.

In over 300 operations on the modified Paul-Mikulicz plan Lahey (1942), who has done so much to popularize this procedure and to whom I am indebted for much valuable advice, did not have a single case in which closure of the faecal fistula showed any signs of failure. I can say the same for my small series of cases.

Rankin (1942) voices the view of the opponents of the Paul-Mikulicz operation by stating that "few circumstances are more unpleasant to a convalescent patient than a deluge of liquid alvine discharges over the abdominal wall".

It is true that convalescence with the two-stage operation is more protracted than with resection and sutured anastomosis, and that in the interval between the first and second operations some distress, and in certain cases even apprehension, is occasioned by the discharges of ileal contents on to the skin, which may at times cause severe local searing; but this is the *price*—and in my opinion it is a small one—which the patient has to pay for added safety.

I abandoned primary resection and anastomosis for cancerous lesions of the right colon because my operative death-rate was considerably higher with sutured anastomosis than with the exteriorization-resection method. After performing primary resection and anastomosis, even after taking all conceivable modern precautions before, during and after operation, I was always apprehensive when about to see my patient on the following days; he was either sitting up in bed reading the paper or he was struggling for life. Those that died did so, from peritonitis, or from severe infection of the wound which subsequently broke down.

Patients dislike stage operations, as also the inconvenience—social and economic—which accompanies a discharge of faeces on to the abdomen. They will often insist that they themselves are fully prepared to assume the additional risk of a one-stage procedure, by which they really mean that they will accept the added risk of a one-stage operation provided they do not die.

In 85% of cases death following resection of the colon is due to ileus or peritonitis. The Paul-Mikulicz plan almost entirely eliminates these lethal complications, as the ileum is immediately decompressed following the resection of the bowel, and at the second stage the anastomosis is made extraperitoneally, thus avoiding the danger of peritoneal contamination. We now possess sufficient statistical evidence to show that the Paul-Mikulicz procedure is associated with a considerably lower operative mortality

OUTLINE OF OPERATIVE TREATMENT

Patients presenting themselves for treatment fall into four groups: (1) Acute obstruction; (2) chronic obstruction; (3) perforation of the growth with: (a) local abscess; (b) spreading peritonitis; (4) no obvious obstruction.

Acute Obstruction

In every 10 cases of colonic obstruction, 9 are due to carcinoma; obstruction in the left half of the colon is eight times as frequent as obstruction in the right half.

Approximately 30% of the cases of carcinoma of the colon give rise to acute or subacute intestinal obstruction, which of itself has a mortality of 20%. Acute obstruction of the colon is a surgical emergency, and some type of decompression should be carried out expeditiously to forestall perforation of the cæcum. An attempt should be made before operation to determine as accurately as possible the site of the blockage by means of straight X-ray pictures as well as by clinical methods.

I am entirely opposed to exploration of the abdomen in the presence of acute obstruction of the colon. The exploring hand thrust among the tensely distended coils of bowel produces shock and may lead to perforation of the gut or light up an acute peritonitis, and always causes widespread adhesions between the coils of intestine.

Strangulation of the colon can be excluded by clinical methods, straight X-ray pictures, and inspection of the fluid which escapes when the peritoneal cavity is opened. If this fluid is blood-stained or if a volvulus of the sigmoid loop cannot be ruled out, then judicious inquiry by sight and touch is warranted.

If the obstruction is in the distal colon, a blind loop colostomy should be fashioned above the umbilicus through a right transverse muscle-cutting and retracting incision, and the bowel should be deflated by intermittent suction through a wide-bore needle. A few hours later, when the colon is sealed to the wound, a longitudinal incision is made in the bowel to allow the pent-up feces to escape.

When the obstruction affects the proximal colon, a satisfactory decompression can sometimes be accomplished by means of a Miller-Abbott tube or an indwelling intestinal tube attached to a continuous-suction apparatus; but should this simple expedient fail, a valvular tube cæcostomy should be performed under local anaesthesia through a small right McBurney incision. For obstructive lesions of the ileo-cæcal valve or the cæcum, suction applied to a Miller-Abbott tube is safer and more effective than tube ileostomy.

Chronic Obstruction

Chronic obstruction of the mild variety can almost always be corrected by copious bowel washouts, saline purgatives, and the administration of large doses of succinyl sulphathiazole which is a potent laxative and bacteriostatic drug.

Primary resection and anastomosis should never be undertaken even when the bowel is only moderately distended; on the other hand, exteriorization-resection is a safe procedure, as after removal of the malignant mass the bloated proximal limb of colon forming the double-barrelled colostomy can be decompressed immediately.

Perforation of Carcinoma of the Colon Associated with Abscess Formation or Spreading Peritonitis

No type of resection should be attempted in the presence of frank suppuration. In such cases the faecal current should be deflected from the necrotic cancerous tumour by the performance of a loop or a divided Mikulicz colostomy, and the abscess or peritoneal cavity drained and powdered with sulphadiazine. When the infection has subsided, the abdomen should be explored, and if resection is feasible this should be undertaken (on the now cleansed, debacterialized and defunctioned gut) by the closed (aseptic) oblique end-to-end method of intestinal anastomosis. The defunctioning colostomy is closed two weeks later by the extraperitoneal method.

Resectable Non-Obstructed Carcinomata of the Colon

I.—*Carcinoma of the proximal (right) colon.*—For non-obstructing resectable malignant tumours involving the last loop of ileum, ileo-cæcal valve, cæcum, ascending colon or hepatic flexure, the majority of surgeons would perform a one-stage or a two-stage intraperitoneal operation, i.e. (a) hemicolectomy followed by anastomosis between the terminal ileum and the transverse colon; or (b) preliminary ileo-transverse-colostomy followed two or three weeks later by wide excision of the involved colon.

There would, of course, be differences of opinion among surgeons concerning the open and the closed (aseptic) methods of anastomosis, and over the relative merits of the end-to-end, side-to-side and end-to-side types of junction. Resection with sutured anastomosis for tumours of the right colon is without any question a time-honoured, well-standardized and radical operation which is widely practised with good results by

Dr. Cuthbert E. Dukes: I have reviewed the pathological findings in operation specimens from 331 cases of cancer of the colon. The result does I think show that, in so far as pathological considerations are concerned, the general prospects of surgical treatment should be exceptionally good.

There are two interesting peculiarities of colon cancer.

The first is the unequal sex distribution. In the proximal end of the colon, cancer is more common in women than in men, but in the distal end this ratio is reversed, so that in the pelvic colon and rectum cancer is much commoner in men than in women. This analysis is based on operation specimens but a very similar unequal sex distribution is recorded by the Registrar-General for England and Wales, the figures in this case being based on death certificates. The correspondence between the two series is almost identical for right half of the colon and rectum but is not so close for cancer of the intermediate regions, the operation cases showing a slight predominance of males and the death certificates a slight increase in females.

A second peculiarity of cancer of the colon of practical surgical importance is its unequal regional distribution. In general, cancer is much more common at the distal than at the proximal end of the colon. In the series of 331 operation cases there were 75 in the right colon (including cæcum, ascending, and right half of the transverse colon) and 256 in the left colon (including the left half of the transverse colon, splenic flexure, descending and pelvic colon). During the period when these patients with colon cancer were being treated the same group of surgeons performed more than 1,000 operations of excision of the rectum for cancer.

This increase in the incidence of cancer on passing distally from the cæcum to the rectum may be related to the rate of flow of the intestinal contents which is comparatively rapid in the right colon, slower in the left colon and almost stationary in the pelvic colon and rectum. We know from the results of experimental cancer research that the onset of malignancy is influenced both by the concentration of a carcinogenic agent and the period of its action. If cancer of the colon is due to a carcinogenic agent present in the faeces its influence would certainly be greatest towards the distal end of the colon because of the slower passage and greater concentration of the intestinal contents.

There is a close general resemblance in the microscopic structure of malignant tumours from different regions of the colon but I think also that slight differences may be detected, some of which are of surgical interest. These are brought to light when tumours are graded on the basis of their histology. It is a well-established principle of pathology that anaplasia or lack of differentiation of cancer cells is a sign of rapid growth, and conversely well-differentiated tumours tend to grow more slowly. This is the basis of Broders' method of grading which, though not applicable to all forms of malignant disease, is certainly of value for intestinal tumours. I have used this system of grading for all the 331 cases of colon cancer and made a comparison with a similar but larger series of 1,000 cases of rectal cancer in which follow-up records were available for more than five years. In rectal cancer the ultimate prognosis after operation is clearly related to the histology of the primary tumour and there is no doubt that patients with well-differentiated Grade I tumours have the best prospect of survival after operation. These tumours of a low grade of malignancy are relatively commoner in the colon than in the rectum. Grade I tumours form 16% of colon cancer but only 6% of rectal cancer. Moreover a general comparison of the histology of colon with rectal cancer shows that on the whole growths in the colon are better differentiated histologically than those in the rectum.

This suggests that malignant growth proceeds more slowly in the colon and this opinion is supported by the fact that venous and lymphatic spread are less commonly found in operation specimens of colon cancer than in rectal cancer. If a dissection is made of the veins of operation specimens clumps of cancer cells can be found within the veins of about 17% of cases of rectal cancer but in only about 12% of growths in the left colon and 6% of those in the right colon. Lymphatic metastases are also less commonly found in cancer of the colon than in cancer of the rectum. During the years covered by this review lymphatic metastases were found in between 50 and 60% of cases of rectal cancer but only in from 35 to 40% of cases of colon cancer. The evidence from these three sources—the histology of the primary tumour, the extent of venous spread and incidence of lymphatic metastases—all leads to the encouraging conclusion that cancer of the colon is a relatively favourable field for surgical treatment. In a recent analysis (Dukes, C. E., *Proc. R. Soc. Med.*, 1944, 37, 131) I have shown that rectal cancer can be cured by surgery in approximately half the cases now being treated by radical excision, but for the reasons just stated I should expect the end-results of surgery of colon cancer to be considerably better.

and that the late results are on the whole as good as, or even better than, those which follow the intraperitoneal operation. In support of this statement I would refer you to the brilliant Presidential Address given by Mr. Zachary Cope (1940).

No removal of carcinoma of the colon with immediate suture has been carried out in the Lahey Clinic now for over thirteen years. The surgeons at that Clinic have performed over 300 Paul-Mikulicz operations with a mortality of about 10%; but in 100 excisions of growths of the proximal colon there were only three fatalities. In a personal series of 60 cases there were six deaths—10%, and in 21 excisions of the right colon there were two deaths—just over 9%. Following removal of the growth and its related mesentery the blood supply to the remaining segments of bowel must of course be carefully preserved. This is true of any type of bowel resection, although it should be pointed out that in the Paul-Mikulicz operation necrosis of the distal $\frac{1}{4}$ in. or $\frac{1}{2}$ in. of either segment will not produce a fatal peritonitis, as it is likely to do following an intraperitoneal anastomosis.

Papillomata are found near the primary growth in over 75% of cases and may be distributed far afield. The exteriorization-resection operation enables the surgeon to inspect by direct vision large segments of the colon, and if any polypi are seen, these may be successfully fulgurated through a sigmoidoscope, thus improving end-results by diminishing the risks of a second primary cancer coming to light in another part of the bowel.

II.—*Carcinomata of the distal (left) colon.*—There are two good stage-operations for removable cancers of the left bowel: (a) *The Paul-Mikulicz operation* which here has its widest and most popular application; and (b) *Defunctioning Colostomy* followed later, when the colon has been effectively cleansed, by resection and oblique end-to-end closed (aseptic) anastomosis. The final stage consists in closing the colostomy—which may be of the loop variety (in acute obstruction) or be fashioned on the modified Devine plan without the intervening layer of skin between the stomas.

III.—*Carcinomata of the last few inches of the sigmoid colon and of the recto-sigmoidal region.*—For growths in these situations the surgeon may elect: (1) Miles's abdomino-perineal excision; (2) Hartmann's abdominal resection of the rectum with permanent colostomy; (3) the abdomino-anal operation so ably practised by Lloyd-Davies; or (4) abdominal segmental resection of the recto-sigmoid segment with sutured anastomosis preceded by a divided Mikulicz type of colostomy.

The last-mentioned operation would appear to be particularly indicated (a) when the cancer involves the lower reaches of the sigmoid loop and the vascular field is not obscured by fatty tissue; (b) in poor-risk patients; and (c) when permanent colostomy is refused.

So-called conservative resection operations for cancers arising in the recto-sigmoid, which aim at sparing the levatores and sphincter apparatus, are becoming increasingly popular since it has been demonstrated by Dukes, Collier and others that the spread of cancer along the lymphatics from this region is upward.

CONCLUSIONS

(1) The modified Paul-Mikulicz operation is the one of choice for both proximal and distal segments of the colon and is in every respect as radical and thorough as resection with sutured anastomosis.

(2) It has a lower mortality than resection and sutured anastomosis as the danger of peritoneal contamination is largely eliminated.

(3) Resection with sutured anastomosis is justified only when the colon has been efficiently defunctioned by a preliminary colostomy.

(4) The staging of operations for carcinoma of the colon has been the most important contribution to surgery of the colon during recent years.

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where careful dissection will be necessary to determine accurately the course of the main vascular trunk. The vascular pedicle with its accompanying lymphatics draining the area of the growth is then divided at its origin from the main vessel. No further dissection than this can be made unless the main inferior mesenteric trunk be taken, in which event a resection of the upper half of the rectum becomes inevitable. The same principle applies to other parts of the left and transverse colons. Care must be taken at each division of vessels to note that the bowel to be left has an adequate blood supply. There is no rule of thumb in deciding this point, no Sudeck's or Hartmann's critical angle. The vessels in every case will vary and accurate observation alone is the only safe guide. The limbs of bowel proximal and distal to the segment being resected are now brought together and a continuous suture approximates two convenient *tæniæ coli*. If it is found that there is insufficient bowel further mobilization may be necessary. In the case of a sigmoid resection the splenic flexure may have to be detached and swung downwards towards the pelvis and in that of the transverse colon hepatic and splenic flexures may be freed. It is important to make as long a gun-barrelling as possible, three inches being the least amount to be aimed at. For the pelvic colon a left oblique muscle cutting incision is very satisfactory but because of the shallow character of the left iliac fossa the two limbs (gun-barrelled) should be placed obliquely to the surface. The deficiency or rent in the mesentery is now repaired and any other raw peritoneal surface covered. The parietal peritoneum is closed allowing sufficient room for one finger to be passed comfortably alongside the gun-barrelled loops. The upper margin of the gun-barrelling suture and viable colon should reach outside the closed peritoneum. The remainder of the wound is closed in layers with interrupted sutures. Sulphathiazole powder is insufflated into each layer. The surface is sealed with gauze soaked in Whitehead's varnish and superficial dressings applied.

The bowel to be resected is now divided between either Parker Kerr or small Payr's clamps, the clamp on the distal loop being applied in such a way that it can be left in situ comfortably on the abdominal wall. This clamp retains the two limbs of bowel on the surface and it is advisable not to divide the bowel flush with this clamp but to leave $\frac{1}{4}$ to $\frac{1}{8}$ in. of bowel above it. This will prevent slipping which is especially important should there be a slight amount of tension. The treatment of the upper limb will depend on the amount of spare bowel. If in excess, division can be made well above the skin surface, the clamp removed and the bowel left open. If short, it is advisable to tie in a rubber catheter for twenty-four to forty-eight hours until the bowel becomes adherent. Vaseline gauze tucked round the bowel between it and the subcutaneous tissues will aid adhesions and help to form an adequate barrier to infection. In obese subjects with a short mesentery, the excision of subcutaneous fat around the wound, so bringing the level of skin nearer to the aponeurosis will often be found essential.

The distal clamp is removed in five to seven days, the lower limb opened and the enterotome applied. A note should be made at operation of the position of mesentery in relation to the suture opposing the two limbs of bowel and the enterotome applied away from the mesentery.

The enterotome will be loose by the fifth to seventh day and when assessing the bite it must be remembered that the anastomosis formed by it is of recent origin and easily perforated by rough examination. A further application if required is best postponed for seven days. Ideally, three inches of spur division is necessary, and the division must be below the level of the peritoneum.

Closure of the colostomy may occur spontaneously if the mucous membrane is beneath the skin level, but more frequently a formal closure is desirable to prevent a ventral hernia. The optimum time for this is two to three months later when complete healing of the wound has taken place and the tissues are pliable. If done earlier the difficulties and risks are greater.

The principle of closure as with original division of the bowel is that it should be extraperitoneal. Preliminary bowel washouts and pulv. catechu. co. 1 drachm three times a day are given for two days. Two inches or so of the original scar above and below the colostomy are excised with a thin lip of skin around the stoma. The aponeurosis and muscle are defined and the adhesions between these and the bowel carefully dissected while traction and counter-traction are made. By this means the bowel is lifted free of attachment to skin, aponeurosis and muscle. Any inadvertent opening of the peritoneum must be closed immediately. The lip of skin and fibrous tissue left on the stoma are now removed. Outward rolling of the edge of the stoma is quite commonly seen and this should be dissected free by undercutting to enable an invaginating suture to be inserted effectively. One continuous Connell suture is usually quite adequate

Mr. O. V. Lloyd-Davies: The series of cases which I am presenting are those dealt with in the ten-year period 1934-44 from St. Mark's and one of my other hospitals. They are cases involving the transverse and left colons only.

In all there are 73 cases of resection. The operability rate was 60%, the remaining cases being turned down chiefly on account of multiple liver and peritoneal deposits.

The average age was 56.5, the oldest being 78 and the youngest 28. The operative mortality-rate, which includes all deaths within one month of the operation, was 4.1%, the three deaths being due to cardiac failure, cerebral thrombosis and wound sepsis. Included in the series are 6 cases requiring small gut resections at the time and one case of partial gastrectomy, all of whom survived operation, the latter being alive over eighteen months later. An analysis of the cases from the point of view of degree of spread at the time of operation shows that approximately 38% had glandular metastases as compared with 60% in carcinoma of the rectum. Of this series 10 are untraced, leaving 60 cases of whom 11 have died of recurrence and 7 from other causes. Of these 11 deaths, 8 had glandular metastases at the time, and of the remaining cases, one had a palliative operation, there being liver deposits, and one showed invasion of a vein. The third had extensive pericolic spread requiring small gut resection.

This series is not large enough to produce figures of value on a five-year cure basis, but as far as it goes it indicates that the operation is safe and that a most important feature of any operation for carcinoma of the colon should be an adequate clearance of the tissues containing the lymphatics draining the involved bowel.

Preliminary accurate diagnosis of the position of the tumour by barium enema is most essential, remembering that this method may fail in the lower pelvic colon, where the sigmoidoscope will be of invaluable use. A barium meal may be dangerous and can convert a chronic into an acute obstruction. For the acute obstructions, after a plain X-ray of the abdomen to locate the growth, a blind cæcostomy of the valvular type should be done, followed by investigations later. This type of cæcostomy works well provided regular irrigations are given through the tube. A thorough general physical examination must then be undertaken together with electrocardiography where necessary. Blood-count and grouping, blood urea and urine estimations have been routine, and the hæmoglobin should be not less than 85% before the operation. A course of sulphasuxidine given for four days before operation sterilizes the bowel contents of *B. coli* organisms. 20 grammes per day appears to be the optimum amount and it should be given as a routine.

The anæsthetic in the majority of these cases has been controlled spinal anæsthesia—heavy nupercaine 1/200 was used with control of blood-pressure by means of the adrenaline drip method introduced by Dr. Frankis Evans.

With regard to incisions—for the pelvic colon a left oblique muscle cutting incision is very suitable in thin subjects and left lower paramedian in the obese. For the splenic flexure and descending colon a left transverse incision retracting the rectus medially or dividing it as the case demands, and an upper paramedian incision for the transverse colon.

The operation performed in all these cases goes under the name of the Paul or Mikulicz operation but differs in certain important details from the original descriptions. Briefly Paul's method was to resect the appropriate portion of bowel within the abdomen, to tie into the proximal and distal limbs an angled glass tube and then to gun-barrel the limbs and close the abdomen. The spur was crushed with an enterotome in the usual way at a later stage, and in the final stage the surface bowel was turned in and the skin only sewn over. The criticisms of this method were that a radical removal of the lymphatic field was not made and there was a risk of sepsis by intra-peritoneal division of the colon.

Von Mikulicz's method was to mobilize the involved bowel, bringing it above the surface of the abdominal wall without dividing the mesentery. The wound was then closed and a week later the extraperitonealized loop was removed. The later stages were similar to Paul's operation. This method overcame the intraperitoneal division of the bowel but was probably even less radical from the point of view of lymphatic spread. It had a further defect in that secondary deposits occurred in the wound due to the growth being left in situ.

The method adopted in all cases in the series now reported has overcome the criticisms of these older and original operations. The involved bowel is well mobilized by dividing all peritoneal attachments—this is particularly well demonstrated in the sigmoid colon where multiple peritoneal folds will be found lightly attached to the outer side of the mesentery. These are carefully divided and the mesentery gradually raised from the iliac fossa. The vessels must then be clearly defined and this will be aided by transillumination, but it may be a troublesome task in a fat-laden mesentery,

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

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Steatorrhœa due to Lymphatic Obstruction

By R. S. BRUCE PEARSON, D.M., F.R.C.P.

THE syndrome associated with the passage of fat in the stools is of exceptional interest both because of the difficulties of differential diagnosis and the still greater difficulty in understanding the pathological basis for the biochemical abnormalities which develop secondarily. The following table shows briefly the conditions in which fat may be found in excess in the stools:

STEATORRHŒA			
Sprue	Hillary	1776	
{ Non-tropical sprue	{ Richartz	1905	
{ Idiopathic steatorrhœa	{ Thaysen	1924	
{ Adult cœliac disease	Gee	1888	
Cœliac disease	Gull	1855	
Steatorrhœa due to lymphadenopathy	Whipple	1907	
Intestinal lipodystrophy	Glyn & Rosenheim	1938	
Steatorrhœa with chyladenectasis			
Pancreatogenous steatorrhœa			
Gastrocolic fistula with steatorrhœa			

The lipodystrophy of Whipple and the chyladenectasis of Glyn and Rosenheim are both great rarities which will not be discussed further. Pancreatogenous diarrhœa, which may be very difficult to differentiate from the sprue syndrome, will also not be considered more fully, nor will the steatorrhœa found in gastrocolic fistula.

There remain tropical sprue, idiopathic steatorrhœa, cœliac disease and steatorrhœa due to lymphadenopathy. Thaysen, in his monograph "Non-tropical Sprue", maintains that the first three of these conditions are identical, varying only with the age of the patient and environment in which the condition is acquired. There are objections to this view but the clinical picture has many features in common. Izod Bennett and Hardwicke have drawn attention to the widespread disturbance of metabolism encountered in these conditions of uncertain pathogenesis. In the following table the main symptoms of idiopathic steatorrhœa are shown with the biochemical abnormalities or disturbance of function that give rise to them.

IDIOPATHIC STEATORRHŒA

General Symptoms: Diarrhœa, fatigue, loss of weight, pigmentation.

Biochemical abnormality	Corresponding symptoms or signs
High faecal fat	{ Bulky, pale stools. Dilatation of small intestine and colon. Metecrism.
Low serum calcium	{ Tetany. Osteoporosis with loss of weight.
Low serum protein	Edema.
Flat sugar tolerance curve	

Other associated abnormalities of function:

Failure to absorb	
Iron	Microcytic anemia
Castle's factor	Macrocytic anemia
Vitamin B complex	{ Red smooth tongue, stomatitis Cheilosis Pellagra-like lesions of skin

That a somewhat similar symptom complex can arise as a result of obstruction of the lacteals has long been recognized. As already mentioned Gull drew attention to this in 1855. Ryle published two cases in 1924 in which tuberculosis of the mesenteric glands was associated with a long-standing history of steatorrhœa. In a recent paper (1944) Klein and Porter described a very remarkable case in which there was eventually failure to absorb fat, carbohydrate and protein due to tuberculosis of the mesenteric lymph nodes. Hamilton Fairley and Mackie, who have recorded cases in which lacteal obstruction was due to Hodgkin's disease and to lymphoma point out how difficult the differentiation between tropical sprue and steatorrhœa due to lymphadenopathy may be.

for the closure supplemented by the oversewing of any adjacent appendices epiploicae. An additional Lembert suture can be used if there is doubt but it must be remembered that every additional row reduces the lumen of the bowel. I have been called in to reconstruct two cases where there had been inadequate spur division and excessive inversion of the bowel by over-suturing. The closed bowel if adequately freed in the first instance should now lie comfortably below the level of the muscle of the abdominal wall which is then closed with interrupted sutures—a small drain being placed down to the bowel. The tissues in the vicinity of the colostomy appear to be well vaccinated against bowel organisms but the addition of sulphathiazole is of value for healing.

POST-OPERATIVE CARE

It is inadvisable to allow fluids by mouth until normal peristalsis has returned and during this interval adequate fluids must be given by other routes. In most of these cases intravenous saline and glucose were given in the proportion of one part normal saline to four parts isotonic glucose and the amount being 3 to 3½ litres per twenty-four hours. These amounts supply the correct quantity of fluid and salt which the body needs and the glucose is a make-weight for isotonic purposes and is also of nutritional value. Normal peristalsis usually returns in forty-eight hours, and provided flatus is being passed there is no urgency to get the bowel to act and no aperient or wash-out should be given for five to seven days.

COMPLICATIONS

Apart from cardiac and pulmonary complications, the particular troubles affecting this operation are: First, wound sepsis, which has been much reduced by powdering the layers of the wound with sulphathiazole. This will, I think, be still further reduced by the use of sulphasuxidine. Inadequate blood supply to the limbs has fortunately not caused deaths in this series but has been responsible for wound sepsis. The blood supply should be most carefully noted at operation. Second, paralytic ileus has become less frequent by withholding fluids by mouth until the return of normal peristalsis.

In conclusion, pathological examination of all specimens in this series shows that this is an adequate operation for the disease and as radical as any intraperitoneal resection. It is safe and post-operative worries are infinitely less for both patient and surgeon.

This method can be applied most satisfactorily to the whole of the transverse and left colon with the exception of the recto-sigmoid area. In thin subjects with a long pelvic loop a satisfactory Paul-Mikulicz type operation may sometimes be accomplished.

The alternatives can be divided into two groups: (1) Those aiming at restoration of the continuity of the bowel; (2) permanent colostomy methods.

In the former group (1) Intraperitoneal resection and anastomosis preferably with defunctioned bowel; (2) a Devine type restoration after a Hartmann's operation; (3) an abdomino-anal excision.

In the second group (1) Hartmann's; (2) combined excision.

This area merits a discussion for itself.

With regard to the right colon our series is not large enough to be of statistical value. A complete extirpation of the ileo-colic and right colic trunks is necessary and a side-to-side ileo-transverse colostomy gives good results because an adequate stoma can be made.

The contents of the bowel are fluid and the contractive power of the right colon much less than the left colon.

I have performed the Paul-Mikulicz type of operation on this side, advocated by Lahev, on only four occasions and from my small experience its main disadvantage is the skin excoriation with delayed healing.

The skin can be kept in a good state for the first five or six days with a tied-in soft catheter attached to a low-pressure suction apparatus but the difficulties arise when the enterotome is applied. I think it is an advantage to gun-barrel ileum to colon for at least six inches and crush the spur to a much greater depth than on the left side, a loose-fitting, soft-acting long Spencer-Wells being applied after the initial application of the enterotome.

I would certainly advocate this method in two circumstances: First, in the case of adherent growths in which dissection has been unavoidably prolonged and the patient's condition does not warrant the time necessary for a careful anastomosis. Secondly, in those cases in which the degree of obstruction is found to be subacute and greater than at first estimated.

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[April 24, 1945]

Steatorrhœa due to Lymphatic Obstruction

By R. S. BRUCE PEARSON, D.M., F.R.C.P.

THE syndrome associated with the passage of fat in the stools is of exceptional interest both because of the difficulties of differential diagnosis and the still greater difficulty in understanding the pathological basis for the biochemical abnormalities which develop secondarily. The following table shows briefly the conditions in which fat may be found in excess in the stools:

STEATORRHŒA			
Sprue	Hillary		1776
Non-tropical sprue	Richartz		1905
Idiopathic steatorrhœa	Thaysen		1924
Adult cœliac disease	Gee		1888
Cœliac disease	Gull		1855
Steatorrhœa due to lymphadenopathy	Whipple		1907
Intestinal lipodystrophy	Glyn & Rosenheim		1935
Steatorrhœa with chyladenectasis			
Pancreatogenous steatorrhœa			
Gastrocolic fistula with steatorrhœa			

The lipodystrophy of Whipple and the chyladenectasis of Glyn and Rosenheim are both great rarities which will not be discussed further. Pancreatogenous diarrhœa, which may be very difficult to differentiate from the sprue syndrome, will also not be considered more fully, nor will the steatorrhœa found in gastrocolic fistula.

There remain tropical sprue, idiopathic steatorrhœa, cœliac disease and steatorrhœa due to lymphadenopathy. Thaysen, in his monograph "Non-tropical Sprue", maintains that the first three of these conditions are identical, varying only with the age of the patient and environment in which the condition is acquired. There are objections to this view but the clinical picture has many features in common. Izod Bennett and Hardwicke have drawn attention to the widespread disturbance of metabolism encountered in these conditions of uncertain pathogenesis. In the following table the main symptoms of idiopathic steatorrhœa are shown with the biochemical abnormalities or disturbance of function that give rise to them.

IDIOPATHIC STEATORRHŒA

General Symptoms: Diarrhœa, fatigue, loss of weight, pigmentation.

Biochemical abnormality

Corresponding symptoms or signs

High faecal fat

{ Bulky, pale stools.
Dilatation of small intestine and colon.
Meteorism.

Low serum calcium

{ Tetany.
Osteoporosis with loss of weight.

Low serum protein

Edema.

Flat sugar tolerance curve

Other associated abnormalities of function:

Failure to absorb

Iron

Microcytic anemia

Castle's factor

Macrocytic anemia

Vitamin B complex

{ Red smooth tongue, stomatitis
Cheilosis
Pellagra-like lesions of skin

That a somewhat similar symptom complex can arise as a result of obstruction of the lacteals has long been recognized. As already mentioned Gull drew attention to this in 1855. Ryle published two cases in 1924 in which tuberculosis of the mesenteric glands was associated with a long-standing history of steatorrhœa. In a recent paper (1944) Klein and Porter described a very remarkable case in which there was eventually failure to absorb fat, carbohydrate and protein due to tuberculosis of the mesenteric lymph nodes.

Hamilton Fairley and Mackie, who have recorded cases in which lacteal obstruction was due to Hodgkin's disease and to lymphoma point out how difficult the differentiation between tropical sprue and steatorrhœa due to lymphadenopathy may be.

My purpose in describing the three following cases is further to emphasize the similarity between these two groups of cases—idiopathic steatorrhœa and steatorrhœa due to lacteal obstruction.

CASE I.—The first case is that of a woman aged 45 years, first seen in April 1942. She complained of a sore tongue which she had had for eighteen months—due to numerous aphthous ulcers affecting the tongue and gums. She stated that she had suffered from attacks of diarrhœa over a number of years. On investigation she was found to have a macrocytic anæmia and a high faecal fat. Investigations carried out at this time were as follows:

Total	Faecal fat % Split	Unsplit	Hb %	C.I.	B.S.R.	Total	Serum Protein % Alb.	Glob.
50%	32%	27%	76%	1.1	10 mm.			
43%	23.0%	10.4%	82%	1.28		6.3%	3.6%	2.7%

After six months erythema nodosum developed, the B.S.R. rose from 10 mm. in May to 17 mm. in October and 30 mm. in December. There was a slight irregular temperature. A chest X-ray at this time showed enlarged mediastinal glands and a small bunch of glands appeared above the left clavicle. These were removed for section and showed the following characteristics reported by Dr. Duncan Clay: "The whole gland is occupied by bulky rounded masses of epithelioid appearance. Very occasional giant cells can be found. There are a number of irregular areas of somewhat atypical caseous necrosis. The cell masses are separated by narrow zones of lymphoid tissue. The diagnosis appears to rest between an atypical tuberculous reaction and Boeck's sarcoid." It was concluded that a similar condition affected the mesenteric glands.

The Mantoux reaction was positive to 1:1,000 O.T. in December 1942. A diagnosis of tuberculous lymphadenopathy was made in this case, although the late development of erythema nodosum was difficult to explain. Treatment was with vit. B, plexan, calcium and radiostol. The tongue condition was rapidly relieved but the anæmia was refractory and only slightly improved. Now, after three years, she is symptomatically well although the recent hæmoglobin is only 82%. A blood-sugar curve carried out this year was within normal limits. A radiograph of the chest now shows that the enlarged root-glands have returned to normal size.

This case had the following features in common with idiopathic steatorrhœa: (1) High faecal fat; (2) sore tongue; (3) macrocytic anæmia. Tetany was never demonstrated. The diagnosis in this case depended on the appearance of glands above the clavicle, the irregular pyrexia, and the chest X-ray.

CASE II.—D. E., a boy, aged 15 years. Admitted in February 1940 with a history of diarrhœa of four months' duration. He had recently had some frequency of micturition. He was thin with a prominent abdomen which felt doughy. There was a history of some swelling of the legs for a few weeks at the onset of the condition but this was never present after he was admitted to hospital until shortly before his death a year later.

He did not appear anæmic but the hæmoglobin was 80%, his white blood-count was 9,400 and blood sedimentation rate 4 mm. and 5 mm. An X-ray of the intestine showed that the bowel was closely applied to the lower part of the ascending colon, and that there was some delay in the passage of the meal into the cæcum, the appearance being suggestive of plastic peritonitis. His Mantoux was negative to 1:10. An X-ray of the spine showed changes of Scheuermann's disease (osteochondritis). There was complete achlorhydria.

Total	Faecal fat % Split	Unsplit	Serum calcium mg. %	B.S.R.	Total	Serum protein % Alb.	Glob.	Blood-sugar curve
79.7	50.0	29.7						Resting
83.1	37.8	45.3	6.1	5 mm.	2.9	2.8	0.1	1 hr. after
	On low fat diet							50 grammes
27.6	15.6	12.0	6.8	4 mm.	3.3	2.8	0.5	glucose
					3.25	2.20	1.05	

In spite of the low serum calcium, tetany never developed and Trousseau's sign was persistently negative. He was treated with a low fat diet, calcium gluconate and camphor 2 c.c. daily. He ran a mild intermittent pyrexia up to 99° at first but this fell after six weeks and he became apyrexial. Agglutination tests to the coli-typhoid group were negative.

In February 1941, a year after his first admission, he was admitted with right-sided abdominal pain and passage of blood and mucus in his stools. He was very emaciated, with a high temperature. A mass could be felt in the right iliac fossa. He died shortly after admission.

At necropsy there was a collection of pus in front of the bladder and contained in a thick-walled cavity. The tip of the appendix was included but was not obviously diseased. Some free fluid was present in the abdominal cavity and there were numerous hæmorrhages into the mesentery and the peritoneal coat of the bowel.

The small intestine was contracted and not abnormal. The colon was very thickened and oedematous, particularly in the sigmoid region which was matted to form the wall of the abscess cavity. There were submucous hæmorrhages throughout the colon. Grape-like bunches of cysts containing clear fluid were seen adherent to the peritoneal covering of the intestines—single cysts were also observed.

On section these dilated spaces were found to be lined by a single layer of epithelium and were thought to be lymphatics. Much enlarged lymphatic spaces were seen in the

submucous layer of the small intestines. The mesentery was thickened and œdematous, and the mesenteric lymph glands were difficult to find, and were not enlarged. On section they showed some chronic inflammatory change but no evidence of chyladenectasis.

In this case the high faecal fat, low serum calcium, low serum protein and terminal hæmorrhagic condition, possibly due to failure to absorb vit. K, were all present. The blood-sugar curve was, however, normal, the anæmia only slight and, again, there was an intermittent pyrexia. The dilated lymphatics indicated obstruction to the lymphatic flow although the exact site of this was not demonstrated. The condition was clearly inflammatory in origin and it was presumed that the chronic abscess had arisen before he was first seen and was responsible for maintaining a low-grade inflammatory process with consequent lymphatic obstruction.

CASE III.—F. C., a man aged 55 years, who had complained of weakness and dyspnoea for eleven months. He stated that he had had attacks of diarrhoea off and on since the age of 21. He had had dysentery during the last war. For two months before admission he had had diarrhoea with pain in the left iliac fossa. At times he had cramps in the fingers of a few minutes' duration.

On admission to Leatherhead Hospital in May 1942 he was under the care of Dr. Philip Ellman to whom I am indebted for the notes of his early investigations. He was found to be thin and emaciated, with a distended abdomen. A barium enema showed a greatly distended colon, and this was also seen in the course of a barium meal and follow-through.

	Total	Faecal fat %		Hb %	C.I.	Serum calcium mg. %	Serum protein %			Blood-sugar curve
		Split	Unsplit				Total	Alb.	Glob.	
	32	25.4	7.6	50	1.09	7.1				
1942	41.4	23.8	17.6	40	1.23	7.3				
After treatment				102		9.0				
										Fasting ... 87 mg. %
										1 hr. after 100
										1 1/2 hr. after 98
1945				56	1.2	6.3	4.7	2.2	2.5	1 1/2 hr. after 109
										50 grammes glucose 109

He improved greatly with a low fat, high protein diet, with liver injections, calcium and vit. D by mouth.

He was seen at intervals for the next two years but refused to take any form of treatment and was readmitted in November 1944 with severe diarrhoea and lassitude. His tongue was red and sore; he was generally pigmented. Fresh blood was present in his stools. He had a high swinging temperature. A few days after admission he coughed up blood-stained sputum—a chest X-ray was normal.

His condition deteriorated and he died sixteen days after admission. At necropsy there were purpuric hæmorrhages on legs and arms: the lungs appeared normal except for blood-stained froth in the right eparterial bronchus. The glands at the root of the lung were not enlarged but felt firm and on section showed an appearance suggesting neoplastic infiltration.

The intestines, including the colon, were contracted and did not appear abnormal. The mesenteric glands were small, but one was removed for section.

The microscopical appearance of the bronchial and mesenteric glands was identical and is described as follows by Dr. F. G. Cook: "All showed a loss of normal gland architecture, multiplication of reticular cells, many multinucleate forms, and a fair number of mitoses. In places there was invasion beyond the capsule into the surrounding tissues." A diagnosis of reticulosarcoma was made.

In this case, which simulated idiopathic steatorrhœa in great detail, we have steatorrhœa, macrocytic anæmia, low serum calcium with tetany, low serum protein, flat sugar curve, sore tongue and terminal hæmorrhagic tendency.

These three cases all showed a number of the clinical features usually associated with idiopathic steatorrhœa: in two disease of the lymphatic glands was demonstrated and in the third a chronic inflammatory condition of the bowel and mesentery which was thought to have led to lymphatic obstruction. The flat sugar curve found in one of these cases and the low serum protein in two are of especial interest and indicate that though the primary lesion may be in the lymphatic system, the absorption of food substances other than fat is indirectly affected.

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Dr. Philip Ellman read a paper on "Tuberculous Pericardial Effusion" which will be published in the *British Heart Journal*.

[May 29, 1945]

DISCUSSION: THE PHYSIOLOGY AND TREATMENT OF STARVATION

The President (Dr. Geoffrey Evans) said that the subject of discussion was protein hydrolysate as used in the treatment of starvation conditions found among prisoners of war, the victims of the German concentration camps, and other sufferers from famine in liberated Europe.

The discussion was preceded by an exhibition of photographs showing examples of the physical conditions of those found in the concentration camps, and the projection of two reels of film illustrating the same subject.

In introducing the latter the President said that the Council of the Section had thought that members would like to have the opportunity of seeing these films. They were the same films as were to be seen in the news theatres, but they would furnish the background for the interesting and informative communications which were to be made, one of them by Dr. Janet Vaughan, whom they welcomed on her return from the Belsen camp, where she had been trying out protein hydrolysate and other methods.

The films embodied a certain amount of extraneous matter, such as illustrated interviews with prominent people, but they also showed the recent British delegation of ten members of Parliament visiting Buchenwald camp, and the expression on their faces was more eloquent than a lot of detail of the tragedies they were witnessing. The camera did not shrink from depicting the heaps of dead bodies, all extremely emaciated, nor from obtaining close-ups of the more-dead-than-alive survivors, people reduced to a gaunt and apathetic condition. There was no special medical interest in the films, but they did bring home to the crowded audience the nature of the problem which taxes medical resources to the full.

Dr. H. E. Magee: *Starvation and protein hydrolysates. Physiological considerations.*—In the terminal stages of starvation in man, signs and symptoms related to the gastrointestinal tract are conspicuous features. These are copious and persistent diarrhoea with progressive dehydration and the other effects which follow from the inability to absorb food and fluid.

Observations made by medical men at an earlier period of the war on people in the extreme stages of starvation indicate that the onset of these symptoms almost invariably presages a fatal end, in spite of treatment. The source of this evidence I cannot reveal at present but corroboration has come from China (Laycock, 1944) and from Bengal (Cuthbertson, 1944). Subsequent speakers will give their experience of starvation in liberated Europe. I confine myself to the physiological basis of the symptomatology and of the method of treatment by intravenous protein hydrolysates.

Between 1927 and 1933 I had, with several colleagues, been studying in different animals the functions of the alimentary canal and particularly absorption by the small intestine. Absorption is fundamental to all the other nutritional processes; it is the bottle-neck and if it fails then all the other processes fail too. Failure of absorption seems to me to be the essential lesion in starvation. The experimental evidence I quote points to progressive decline in the efficiency of absorption as the period of fasting is increased; the evidence also suggests that the metabolic processes also suffer.

Cori and Cori (1927) found that glucose and fructose are absorbed by rats more slowly after a forty-eight than after a twenty-four hour fast. This finding was confirmed on several occasions in my laboratory. Here is an example of results obtained (Horne, McDougall and Magee, 1933). The average absorption coefficient for glucose (grammes glucose absorbed per 100 grammes rat per hour) for a group of rats not previously fasted was 0.184; in a group previously fasted twenty-four hours the A.C. was 0.122, the difference (31%) being significant statistically. In the same series of experiments we observed a curious reversal of the effect of atropine on absorption; in non-fasted animals atropine increased the A.C., in animals fasted twenty-four hours atropine decreased it.

Contractions of the intestinal villi are believed to play some part in absorption but what it is precisely has not yet been discovered. Magee and Reid (1931) observed that the movements of the villi are more vigorous in non-fasted cats than in cats fasted twelve hours or more. Working with fowls, Henry, Magee and Reid (1934) showed that the longer the previous fast the lower were the hyperglycemic response and the

specific dynamic action after administering 25 c.c. of 25% glucose. The same dose of glucose always caused diarrhoea in fowls fasted for ninety-six hours or more but, when administered to fowls fasted for seventy-two hours, or less, the whole dose was retained and absorbed. Recently Perakis and Bakalos (1943) found that the hyperglycaemic response to 100 grammes glucose in starving men was abnormally prolonged. These results indicate that deprivation of food, so far from increasing the functional efficiency of the epithelium of the small intestine, actually decreases it; they also suggest that the metabolic functions of the body are slowed by fasting. Corroborative evidence has recently been published by Goettsh *et al.* (1943) who found in animals, after a period of protein deprivation, that amino-acids are removed from the blood much more slowly than in animals fed on adequate diets. It should be remembered that fasts of twelve, twenty-four and forty-eight hours in rats, cats and fowls are equivalent to much longer periods of fasting in man. For instance, a fast of about sixty hours often kills white mice.

Magee and Southgate (1929) had found that the epithelium of the small intestine is endowed with protective functions against the presence of noxious substances (e.g. acids of pH of 1.7) in the lumen. Thus, when the epithelium was devitalized by fluoride or cyanide, the insertion of strong acid solutions into the lumen of isolated segments caused movements to cease at once, whereas when the epithelium was intact, similar solutions were without effect. Evidence pointing towards the same conclusion has also been obtained by several other observers (*see* Magee, 1930, for references).

At the time these absorption studies were proceeding, Dr. T. P. Sun was working in my laboratory on another subject. He (Sun, 1927) drew my attention to work he had done previously on the effects of fasting on the epithelium of the gastro-intestinal tract. He showed that fasts of twenty-four hours or more caused progressive degeneration of the columnar cells of the intestine in white mice. After relatively long periods of fasting, all except the basal portion of the villi became disorganized and degenerated, and, in extreme cases, practically no trace of villi or columnar epithelium remained at all. Provided the degeneration had not gone too far, careful refeeding caused rapid regeneration of the villi. Changes of the same types are referred to in the book by Jackson (1925).

These findings indicate that deprivation of food progressively destroys the digestive, absorptive and protective functions of the alimentary canal and also, it would seem, impairs the metabolic function. The small intestine is the great portal of entry of nutrients into the body and if the essential cells of this viscus are destroyed, as they are in extreme starvation, then the administration of food will act merely as an irritant, causing diarrhoea and withdrawal of water from the body. Therefore, the aim in such cases should be the restoration of the structure and of the function of the intestinal epithelium. Since this cannot be done by giving food by mouth, suitable "building stones" in appropriate amounts must be given by vein. I would emphasize that amino-acids and not whole proteins, e.g. blood proteins, are required, because we must assume that the ability of the starved organism to break down whole proteins would be seriously impaired. Doubtless blood proteins would help in a general way to maintain the patient's vitality but they could not be expected to provide at the required speed sufficient building stones to effect rapid restoration of the damaged epithelial cells. It follows that sufficient glucose should be given, preferably before the proteins, to cover the body's energy needs so as to prevent the amino-acids administered from being used up for energy purposes. It also follows that sufficient B vitamins should be administered at the same time to cover the oxidation of the glucose.

The loss of the protective function of the epithelium lays open the intestine to infection by organisms present in the food and would explain the presence of ulcers so frequently found in persons dying from starvation. The evidence in the confidential report mentioned above dealing with observations on people who had died of starvation during this war came into my hands when, early in 1943, Dr. Gaunt drew my attention to the work of Elman and others in U.S.A. The findings of these observers were to the effect that suitable hydrolysates had been used with considerable success in the treatment of starvation arising out of pathological conditions which prevented the consumption, digestion or absorption of food administered in the ordinary way. Dr. Gaunt showed me a review on the subject which he had prepared. At my suggestion, he published it (Gaunt, 1944). I encouraged him, and subsequently the representatives of another firm, to pursue their researches as vigorously as possible, because I was of opinion that the method of treatment, evidently having proved successful in U.S.A., would be of inestimable benefit to people suffering from acute starvation. At that time

I did not envisage the possibility of cases of starvation requiring this treatment coming to this country, but I was convinced that very many cases requiring it would be revealed when Europe came to be liberated. I said so in a paper I read before the Nutrition Society in March 1944 (Magee, 1944a) and drew attention again to the matter four months later in the *Lancet* (Magee, 1944b).

Dr. Cuthbertson will tell you of the part played by the M.R.C. in this matter and of the progress made in preparing the hydrolysates. I was wrong in my prediction that no cases of extreme starvation would appear in this country. The Ministry of Health has set up emergency supplies of hydrolysate ready for immediate use at headquarters in Whitehall and in the Regional Offices throughout the country.

In the Channel Islands, from which I have just returned, I saw two cases of extreme emaciation in adults. One other case was reported by the Medical Officer of Health of Jersey and all three have been evacuated to this country. They have been referred to Dr. Stannus. I saw about eight other adults, mostly men, and about the same number of German prisoners in varying stages of recovery from nutritional oedema and emaciation. The history of all these cases was in general outline more or less the same. As the diet became more and more vegetarian and therefore more and more bulky and fibrous, the patients became more and more unable to eat food of any sort. Oedema set in and then persistent diarrhoea and sometimes vomiting. In the more severe cases even milk was not tolerated. Before liberation some patients had died and some were operated on for strangulation and intestinal obstruction. A few post-mortems were done. There were observed at operation or post mortem volvulus of the caecum with spastic contraction of the transverse colon and ballooning of the part proximal to it. The large and more rarely the small intestine were thinned out to an extreme degree and seemed to consist mainly of the serous coat. Ulcers of the large intestine were also sometimes seen. These findings seem to fit in with the pathology of starvation as sketched above.

The surgeons on the Islands also informed me that at first perforation of peptic ulcers was relatively common and subinvolution of the uterus has been common throughout the Occupation. They also said that the incidence of appendicitis was much lower during the Occupation than before it. Since the liberation of the Islands the great bulk of the population has been suffering from constipation, sometimes very obstinate. I met the whole medical profession of the Islands and all, without exception, deplored the return to white bread which came in with the relieving forces. They expressed the hope that arrangements would be made for them to be supplied with flour of somewhat higher extraction. They do not wish to return to the coarsely ground wholemeal flour which they had during the Occupation but expressed a preference for a flour about mid-way between the present white flour and wholemeal.

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Dr. D. P. Cuthbertson, *Medical Research Council*: In the absence of all food the body's supply of energy is, after the first day or two, derived from its stock of protein and fat—13% being derived from the former and 87% from the latter. Thus the fat content may largely measure the days of survival. Even in partial inanition body protein will be used up and the extent to which the different organs will be depleted is almost certainly inversely proportional to their importance in survival. Insufficient information exists for us to know exactly the order of priority of the various organs and tissues but it is obvious that the vital organs must be kept functioning.

The plasma protein level is the most accessible index of the state of the body proteins but its interpretation is sometimes difficult unless blood volume studies are also performed.

If facilities are available a nitrogen balance yields more accurate information of the protein state.

To reverse the effects of protein deficiency protein must be given by mouth or, if that route is impossible or hopelessly inadequate, then by vein either as intact protein or in the hydrolysed form. When it was realized that before the body could utilize the protein of the food it must first be split into amino-acids by extensive enzymic hydrolysis, it was but a step to consider feeding the organism with the split products themselves. As long ago as 1913 Henriques and Andersen demonstrated that nitrogen equilibrium and even retention could be attained in the goat when an enzymic digest of goat's flesh was administered intravenously as the sole intake of nitrogen. The therapeutic implications of this did not follow until some twenty-six years later, although the possibility of supplying amino-acids parenterally had been suggested from time to time. In 1939 Elman and Weiner reported the application of a casein hydrolysate to the intravenous alimentation of human subjects and it is interesting that the preparation which they used was an acid hydrolysate of casein refortified with tryptophan (which is lost during digestion with acids) and supplemented with additional methionine or cystine, as these investigators considered that the level of the sulphur-containing amino-acids in casein was not optimal for their purpose. Evidence of utilization, as well as therapeutic effects, were observed by these workers in their patients. Cox and Mueller (1939) next reported that an enzymic hydrolysate of casein containing all the amino-acids of casein was capable of maintaining nitrogen balance and promoting growth. There then followed clinical observations on this product by several American workers. The indications were that it was well utilized, but that reactions might be observed. With improved methods of preparation the occurrence of reactions have apparently almost disappeared and thousands of intravenous infusions have now been given with enzymic (pork pancreas) hydrolysates, particularly of casein, but occasionally also of meat and whole beef-serum (reviewed recently by Martin and Thompson, 1943; Gaunt, 1944; and Cuthbertson, 1944). These reports have mainly referred to studies with one American product "Amigen" which is an enzymic hydrolysate of casein. 100% alimentation with this product and glucose over a period as long as forty days has been recorded by Albright (1944). Other workers have explored the use of papain as the proteolytic enzyme best suited for this work, since its optimum temperature is in the region of 50° to 60° C. at which level bacterial growth is inhibited. Its disadvantage is that the degree of hydrolysis is lower than with trypsin which, in the form of pancreatic extract, produces a more effective degree of splitting but at a temperature which, unfortunately, favours bacterial growth. Beattie *et al.* (1944) have reported success with a casein hydrolysate produced by submitting casein first to the action of papain and then completing the digestion with trypsin. The elimination of pyrogens from pancreatic digests is an extremely difficult problem and requires the strictest aseptic technique. It is for that reason that it has been found safer to test out for intravenous feeding in the present emergencies an acid hydrolysate refortified with L-tryptophan. It is still necessary to determine if an acid hydrolysate fortified with tryptophan is nutritionally as good as an enzymic hydrolysate.

It is obvious that there is no physiological reason for giving protein hydrolysates to patients who can ingest, digest and absorb sufficient protein to serve their actual requirements or at least in amounts sufficient to bring them into a fit state to accomplish this in a reasonable space of time. In view of the risks of reactions and infection it is not wise to submit ill patients to unnecessary forms of treatment. It is therefore only when the patient's capacity to ingest, digest or absorb is seriously affected that the administration of hydrolysates by vein is indicated.

Protein hydrolysates can also be given orally and it was thought they would be suitable in a compact and acceptable form for administering considerable amounts of amino-acids without the fear of pyrogenic reactions. Unfortunately, they are generally unpalatable even to starving men. Casein is a particularly bad offender in this respect; hydrolysed meat protein is less obnoxious. It is possible to mask the taste of these hydrolysates to some extent with suitable flavouring agents, but much more work requires to be done in this field and it may be that with further trials on different proteins or mixtures of proteins more edible digests will be attained. Although intragastric drip may offer a means of overcoming the disagreeable taste, nevertheless this method of alimentation is not exactly a pleasant procedure and I hope that Dr. Vaughan will be able to give you her experiences of this in the field.

There is reason to believe that in starvation the alimentary enzymes may share in the generalized protein depletion and that the power to digest will therefore become affected.

Dr. Magee has already mentioned the changes which appear to take place in the absorptive surface of the intestinal epithelium. The degree to which protein hydrolysates will be effective orally or by stomach tube will obviously depend on the absorptive capacity of the intestinal mucosa and this will vary with the state of the patient. It may be found that if these processes of digestion and absorption are affected *pari passu* the capacity to absorb predigested protein may in effect be not much greater than the power to digest and absorb intact protein. Recent experience does point to the value of skim milk in starvation cases but we must await further information on this from those on the spot.

If amino-acids are supplied without readily available carbohydrate, they will largely be deflected for energy purposes instead of repair. To avoid this it is necessary to cover the energy requirement as far as possible with glucose. It can be given by vein simultaneously with the hydrolysate or by gavage in those too ill to sip. Otherwise it should be given orally so that its absorption coincides with the absorption of the amino-acids. The amount of glucose to be given should be some three times that of the protein. Thus if 50 grammes hydrolysate are given per day the glucose intake should be 150 grammes. This intake provides some 800 calories. If possible double this amount should be given. It may be that deficiency in digestive power and absorptive power will go hand in hand, and if this is so, skim milk plus glucose may well be as effective a line of treatment as the giving of hydrolysates and glucose, and it has the obvious advantage of being less disturbing.

The only report so far published on the use of protein hydrolysates in the treatment of starvation comes from India. Papain digests of meat were used there in the treatment of the starving destitutes of the Bengal famine (Narayanan and Krishnan, 1944; Krishnan, Narayanan and Sankaran, 1944). When given intravenously a considerable measure of success was claimed as the result of intravenous administration of papain digests of meat together with glucose to patients who were too far weakened by starvation even to sip fluids, and that if this line of treatment were followed by suitable hospital diet and care, the death rate was reduced. Even in complicated cases the consensus of opinion was that if the specified treatment was given with hydrolysate and glucose a reduction in death rate occurred. As was natural under the very difficult conditions of this investigation and the pressure of events, a carefully controlled investigation was not possible and the evidence for the favourable effect of intravenous alimentation rests on clinical observation.

During the last few months, before the unconditional surrender of the Germans took place, information from the Netherlands indicated that the food situation of the people there was very grave. There appeared to be grounds for believing that few people in the large towns in N.W. Holland were getting more than 800 cal. per day and that they were probably getting in the region of 400 cal. Further, this very low intake of food was occurring at the end of a long period of steadily dwindling food supply and reports indicated that the strength and endurance of the Dutch people was waning. After considering the data available the Netherlands authorities and the military authorities concerned agreed that the food situation in N.W. Holland was so serious that special measures would be required if a large proportion of the population were to be resuscitated; being impressed by the evidence in favour of the use of protein hydrolysates they invited the Medical Research Council to advise on the provision of suitable preparations in adequate quantity. At the same time a scheme for the application of the emergency treatment was agreed upon with the Netherlands authorities; this scheme included not only the formation of relief teams but also full provision for clinical and laboratory study of the cases of extreme starvation, so that the best method of treatment might be determined without delay. As the result of work carried out during the last eighteen months by its Protein Requirements Committee, the Medical Research Council was in a position to give the necessary technical advice, and in view of the urgency of the need the Ministry of Food and the Ministry of Supply took immediate steps to increase production; with whole-hearted co-operation of the firms concerned the amount of material which was asked for was produced in less than the specified time. Since it also seemed desirable to test the efficacy of plasma and serum in the treatment of extreme starvation, large supplies of these materials were requested and were furnished by the Lister Institute. The work in Holland is now in progress. Representatives of the Medical Research Council and of the Ministry of Food, together with American experts, are acting as scientific advisers at the invitation of the Netherlands Government.

The acute phase in the problem of treatment for extreme starvation may well be over in the next month. It has already concerned a proportion of British prisoners of war and large numbers of occupants of enemy concentration and labour camps. Recently the

Medical Research Council, at the request of the military authorities, nominated a further team of three experts to proceed to the Continent to study the value of protein hydrolysates in the treatment of starvation. Provision has also been made for material to be available for repatriated prisoners of war who may reach E.M.S. hospitals in urgent need of treatment. All these demands have increased the need for medical personnel, and use has been made of Belgian and British medical students who were enrolled, trained, and organized, in anticipation of such a need. Two methods of treatment were envisaged. In the first a 5% solution of protein hydrolysate, which may be prepared by complete enzymic digestion ("Amigen") or by acid hydrolysis and subsequent fortification with tryptophan, was to be given by intravenous infusion. The second method consisted in the administration of the hydrolysate by slow intragastric drip, and in this case the material was to be enzymic digest of casein or meat in which the digestion has not been carried so far. In both cases glucose was to be given in large amount to provide energy and thus to spare the amino-acids for purposes of repair. Vitamins were also provided in the glucose or separately to enable the glucose to be utilized and prevent the development of acute deficiency states. Although it was anticipated that successful treatment should lead within three days to resuscitation to the point at which ordinary food might be taken it was nevertheless obvious that only experience in the field could determine what line of treatment was best.

It is still impossible at the present stage to predict the ultimate value of the protein hydrolysate treatment in extreme starvation. We await further information from our observers in the field and laboratory. The indications are that the lines of treatment which we were called upon to suggest may well require drastic alteration. Apart altogether from the prospect that the availability of protein hydrolysates may provide a possible therapeutic measure in the present medical emergency, the observations which are being made may be expected to have a bearing not only on the immediate problem and that likely to be encountered in the Far East but also on the treatment of all conditions of malnutrition associated with impaired ingestion, digestion or absorption of food over a prolonged period of time.

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Dr. Hugh Stannus: Protein hydrolysates have sprung rather suddenly into some prominence; in fact there are already signs that they might attain the unenviable position of being regarded as a panacea for all ills! This afternoon, however, we are more particularly interested in the use of protein hydrolysates in starvation.

It may not be possible to give a very precise and detailed account of the bodily changes in starvation, but it is known that, associated with the extreme emaciation, there is a marked loss of protein in the tissues—and that to save life the first essential in treatment is to restore protein. The exhibition of protein hydrolysates is only one among other methods which might be employed to attain this object.

Let me briefly recall some of the generally accepted beliefs in regard to proteins and their constituent amino-acids. Proteins are of course the essential constituents of the protoplasm and nuclei of tissue cells. They are also important factors in the osmotic relation between intra- and extracellular fluids and in maintaining the osmotic pressure of the blood. Specific proteins enter into the composition of enzymes, hormones and antibodies. Some twenty to thirty different amino-acids have been isolated from animal and plant proteins. Eight to ten of these are essential for human needs, the quantitative requirements of each being unknown. By combinations of these amino-acids in different order, or in different amounts, or by the omission of some and the addition of others an almost infinite number of different proteins becomes possible. The actual number of proteins is very large—for each kind of animal and plant has proteins peculiar to it; each kind of cell in the tissues of each of the different living beings has its own proteins, differing from those of other cells of the same body.

It has been estimated that there are some 1,600 different types of protein in the body of man. Normally proteins taken in food are broken down in the course of digestion

into their constituent amino-acids. These are absorbed from the gut and pass into the blood-stream whence they are taken up very rapidly by the tissue cells in such proportions as each type of cell requires to build up its own specific proteins.

The amino-acids are the stones or bricks, referred to by Dr. Magee, with which each cell builds its own structure. Normally some proportion of the liberated amino-acids are deaminated by the liver with the formation of carbohydrate. In the absence of exact knowledge upon the subject it was considered probable that in progressive starvation, while some tissues might exercise a priority in regard to any available protein, the functions of the various tissues would one by one fail—among them the functions of digestion and absorption.

Doubt also existed concerning the failure of the complicated systems of enzymes, hormones and antibodies above-mentioned. Again presuming that breakdown and resynthesis would be necessary before any interchange of proteins could take place—for example, between the blood proteins and tissue proteins—the value of supplying the former by means of intravenous plasma appeared uncertain.

The plasma proteins are synthesized by the liver. The total plasma protein is about 7 g. per 100 c.c.; the ratio of albumin to globulin is as 4 to 3. The albumin contributes 80% of the osmotic pressure of the blood due to proteins. The albumin fraction is believed to be the first to be reduced in starvation.

A fall in plasma protein indicates a pronounced loss of tissue protein. It has been calculated that a reduction in plasma albumin from 4 to 3.5 g. % would mean a reduction of the total plasma albumin by 17 g. or one-eighth part. At the same time there would be a loss from the body tissues of at least 510 g. protein. The plasma albumin concentration may return to normal probably long before the protein of the body tissues is made up.

Such briefly was the picture of the conditions in starvation to meet which protein hydrolysate therapy was introduced—a complex picture of many unknowns.

Provided a patient could swallow, and provided he could digest and absorb the requisite amount of proteins, this could be supplied in some suitable form such as reconstituted spray-dried skim-milk powder by mouth, or if he were unable to swallow, then by nasal tube feeding. If he were unable to digest then protein hydrolysate would be given by mouth or by gavage, i.e. a drip nasal feed. Lastly, if he could neither swallow, digest nor absorb, then resort would be had to the intravenous administration of protein hydrolysates.

In practice things are turning out rather differently.

These views were rather shaken in my own case when called upon one evening to advise upon the treatment of a man in an E.M.S. hospital, one from among the first batches of released prisoners of war repatriated to this country.

He was in the last stages of starvation with an extreme degree of emaciation and dehydration, unable to move or converse and, in the opinion of the R.M.O. under whose care he was, unlikely to live through the night. He resembled exactly one of the corpses depicted in the photographs we have seen.

He had a Flexner infection which had failed to respond to sulphaguanidine, or it might be more correct to say that the diarrhoea persisted. His condition had continued to deteriorate in spite of blood transfusion and plasma by vein. He was having difficulty in taking his milk diet. It appeared to be a case demanding intravenous protein hydrolysates. However, at that moment I had none and the case was urgent. Instead, he was given a glucose-saline intravenous drip, a crude liver extract was administered parenterally and teaspoonful feeding with pounded liver substituted for the milk diet. The response was dramatic, the diarrhoea ceased, and one began to wonder whether the use of hydrolysates would not be more limited than as first supposed. A second case responded in a similar manner.

The use of liver is a form of treatment possibly worthy of further consideration. It supplies protein, and probably other important factors, in small bulk and obviates the administration of a large quantity of fluid at a stage when the giving of much fluid will cause oedema and diarrhoea. I believe also that parenteral crude liver extract exerts a specific action in promoting absorption from the bowel.

Among the considerable number of returned prisoners of war detained in hospital I have had the opportunity of examining, signs suggestive of protein deficiency have been almost universal. Many show, besides, all kinds of signs combined into mixed syndromes which one recognizes as indicative of vitamin deficiency. Among these—conjunctivitis,

cheilosis, angular stomatitis, stomatitis, glossitis, changes in the hair, paræsthesiæ, acrocyanosis, altered reflexes, crazy-pavement skin, pellagrous eruptions, &c. Anæmia is common, in some of megalocytic type, and diarrhœa.

Clinical experience and judgment are essential in dealing with these cases, to take but one example—diarrhœa. This may be due to an unsuitable diet, to an infection, to protein deficiency or a deficiency of nicotinic acid.

Drs. Janet Vaughan, C. Dent, and R. Pitt Rivers: *The value of hydrolysates in the treatment of severe starvation.*—At the invitation of 21st Army Group the Medical Research Council were able to send a team out to Europe at the end of April to study the possible value of hydrolysates in the treatment of starvation. Before discussing the scientific results of this study I should like to pay a tribute to the help and encouragement the team received from all the R.A.M.C. personnel with whom it came in contact—particularly to Major-General Phillips, D.M.S. 21st Army Group, to Brig. H. L. Glyn Hughes, A.D.M.S. 2nd Army, and Lieut.-Col. J. A. D. Johnston, Commanding Medical Officer at Belsen. The world has heard a great deal of the horrors of Belsen—it has heard all too little of the gallantry of the handful of men and women, the staff of a field ambulance, a casualty clearing station and a mobile laboratory, who had the courage to tackle one of the most terrible and immense medical problems that has ever arisen. The team arrived late on the field when the worst was over and additional help was coming in, but I shall always feel it was a high privilege to have seen what men and women of goodwill can accomplish in the face of almost unimaginable horror and difficulty.

The scientific problem was twofold: (a) To determine whether hydrolysates were effective in the treatment of severe starvation; (b) to determine whether their use was practical under field conditions. The answer to both questions was in the negative. The materials to be tested can be divided into two groups—one to be given by intravenous injection and one by mouth. The intravenous materials were: (1) Amigen—an American product which is an enzymic digest of casein; (2) an acid digest of casein fortified by tryptophan; (3) serum. The oral materials were: (1) Hydrolysate; (2) spray-dried milk. All were given with glucose and added vitamins. Following the instructions provided by the Medical Research Council for use in the treatment of starvation in Holland, a dose of approximately 50 grammes of hydrolysate was given daily in 2.5% solution in the case of the intravenous preparation for two days and on the third day 25 grammes of hydrolysate was given in the morning followed by 60 grammes of milk powder in the afternoon. Patients on oral hydrolysate received 50 grammes hydrolysate for two days and 25 grammes on the third day followed by 60 grammes milk powder. Patients on milk alone received 120 grammes milk powder daily for three days. On this dosage patients were in negative nitrogen balance and in later observations a higher dosage of oral material was given.

The following investigations were planned: (1) Total plasma protein estimations before treatment began and daily while under treatment. (2) Differential plasma protein estimations and non-protein nitrogen estimations. (3) Estimations of nitrogen intake and nitrogen excretion in both urine and feces. (4) Hæmoglobin estimations. (5) Urine examination. (6) Blood-volume estimations. Under the conditions of work the blood volume estimations were impossible to carry out.

Laboratory facilities in a German hospital were fair. Hospital facilities were primitive. The authorities had taken over for use as a hospital a large well-built but incredibly dirty German barracks. All the furniture had been removed and the rooms were at best furnished with plank beds, straw palliasses and blankets. There were two cold water taps on each floor to serve about 75 patients. The water supply often gave out and then the hospital depended on a cart that might or might not come. Hot water we boiled up ourselves on a rather dilapidated primus stove. For a week there was no artificial light except candles in the investigation ward. One English Sister supervised four blocks containing about 150 patients each, having to help her on each block two Hungarian soldiers, several of the less ill women from the camp and an English R.A.M.C. orderly. The team was extremely fortunate, as it was given two orderlies for day duty and two for night duty. Food was issued from a central kitchen fitted to supply four blocks, and was prepared by Hungarian soldiers and women from the camp under the direction of a Red Cross relief worker or a Sister. Fourteen thousand severely ill people had to be treated under these conditions. It must further be remembered that the majority spoke Russian, Polish, Hungarian or Czech and it was therefore impossible for the medical staff to communicate with them in any way or to reassure them. Patients who were brought into the ward where there was inevitably some apparatus about shouted "nicht crematorium". If a syringe was used to collect samples or an attempt made to

into their constituent amino-acids. These are absorbed from the gut and pass into the blood-stream whence they are taken up very rapidly by the tissue cells in such proportions as each type of cell requires to build up its own specific proteins.

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If intravenous therapy is indicated the results with serum, as already shown, were more promising than those obtained with hydrolysates. This may be due to the fact that to avoid reactions hydrolysates must be given in weak solution and it is therefore not possible to give more than a limited amount of protein without giving too much fluid. It is, however, possible to give relatively large amounts of protein in the form of serum or plasma with little fluid.

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In making this somewhat dogmatic statement it is realized that a peculiar type of patient was being treated, one who had been starved, dehydrated and possibly tortured for a long period, who suffered from many intercurrent infections and profoundly unhygienic living conditions. Hydrolysates may well prove more successful under different circumstances.

Captain J. A. F. Stevenson, R.C.A.M.C., said that he had been asked to take part in that discussion because of some work with which he had been connected at McGill University, Montreal. At that university for two or three years a study, under the direction of Dr. J. S. L. Browne, had been made of metabolic effects of damage, especially in terms of nitrogen balance. Dr. Cuthbertson as well as workers in Canada and the United States had described the very marked increase in the excretion of nitrogen in the urine following fractures, burns, and similar injuries. During this period of increased protein catabolism it had been the experience of most workers that if the intake of protein by mouth were increased very little alteration in the nitrogen balance resulted. As the intake went up the output went up, so that the nitrogen balance was still negative. It was reported by some workers that they could prevent a negative nitrogen balance by the use of protein hydrolysates given intravenously. It had also been noted that following this period of negative nitrogen balance there was a period in which the excretion of nitrogen decreased. This occurred, say in a case of leg fracture, at about the beginning of the second month after the infliction of the injury, the body excreting less nitrogen than it would do on the same intake in health. It was evidently trying to replace the used-up tissue.

At the McGill University Clinic they had administered protein hydrolysate mixtures in both the earlier period of negative nitrogen balance when protein catabolism was predominant and in the later period when protein anabolism was predominant.

Here the speaker showed and explained a chart illustrating experiments with intravenous Amigen. The patients to whom the chart related had been previously healthy and well fed, but had suffered damage in the shape of fractures. It was indicated on the chart that in such cases the amino-acids given by vein were treated by the body in exactly the same way as food given by mouth. Increasing the nitrogen intake by protein hydrolysates intravenously at the height of the protein catabolic period resulted in an increase in nitrogen excretion and during the protein anabolic period in an increased positive nitrogen balance. Those workers who had found that they could prevent a negative nitrogen balance by using Amigen had been for the most part dealing with cases which previously were in a poor nutritional state. In those people there was very little negative nitrogen balance, following an injury. The lesson from the experiments at McGill was to emphasize the probability that there was very little distinction metabolically so far as the body was concerned between the results of giving amino-acids by vein and food by mouth, which was successfully digested and absorbed. Their great use was where food by mouth could not be successfully digested and absorbed.

set up an intravenous drip they again shrieked "nicht crematorium" and curled up shaking in the bed. It had been the habit in the camp for the doctors to inject people with benzine or petrol when alive to induce a temporary paralysis so that they could be taken to the crematorium as dead. As it was impossible to explain our friendly intentions work was made difficult by this terror on the part of the patients.

When the team arrived patients were being admitted from the camp at the rate of 700 to 1,000 a day. They came straight into the human laundry about 20 at a time where they were placed on slabs, scrubbed down to remove the caked dirt and faeces of months and dusted with D.D.T. Here a selection of those thought suitable for further study was made. Men who were so weak that they had to be lifted from the stretchers on to the slab, who were grossly emaciated or else had generalized famine oedema, and as far as could be judged had neither typhus nor tuberculosis were chosen. Oedema of the feet was almost always present, and diarrhoea was extremely common, often so severe as to lead to incontinence. It was impossible with the facilities available to culture more than a random sample of faeces; the majority of cultures proved negative. When patients were, for administrative reasons, not being admitted from the camp, extremely ill patients from those already in the hospital blocks were chosen. The initial plasma protein figures were low on all the patients examined—the mean on 10 patients with generalized oedema was 3.84 ± 0.93 compared with a mean of 4.99 ± 0.78 on the group without gross oedema. The mean figure for albumin on the oedematous group was 2.09 ± 0.46 compared with a figure of 2.79 ± 0.43 on the non-oedematous. In only one instance was there a gross disturbance of ratio.¹

Hemoglobin figures in the men were surprisingly high. The estimations were made with a Sahli instrument which has not yet been standardized. The mean figure for 21 men was 66.5%. This includes three low figures of 27%, 30% and 38% and one high figure in a collapsed dehydrated patient of 128%. Excluding these four figures the mean was 69.0%.

RESULTS

Five patients were given Amigen by the intravenous route. Four did well, the fifth—a patient with famine oedema—showed no improvement.

Three patients were given acid hydrolysate by the intravenous route. Two showed slight, if any, improvement and one—a patient with gross oedema and ascites—became much worse. His abdomen became grossly distended and he developed moist sounds all over his chest. He was then given two litres of concentrated serum over a twenty-four-hour period with the hope of raising his serum proteins. The ascites was considerably reduced and his general condition improved. Three patients showed great improvement on serum; two were given serum in normal concentrations and one 2 × concentration. There was loss of oedema and an increase in general strength and well-being.

An attempt was made to treat seven patients with oral hydrolysate. This material has an extremely unpleasant and persistent taste. To obviate this it has been suggested that a stomach or nasal drip should be used. The Belsen patients, however, regarded the tube as a new form of torture, and only two were persuaded to take it. One died on the second day—the other at the end of two and a half days was definitely worse. The diarrhoea was more severe, the oedema was no better and he was more apathetic and difficult than he had been on admission. A third case took a double dose for two and a half days by mouth. The oedema of his face improved somewhat but the ascites and the oedema of his feet and legs did not. He was no stronger. A fourth case had oedema and ascites but no diarrhoea when first seen. The second day on a double dose of oral hydrolysate he passed half a bucket full of watery, brown faeces containing on analysis large amounts of different amino-acids, he had severe colicky pain and increased ascites. He was therefore transferred to milk diet. Two further cases refused to take more than a small amount of hydrolysate and were given milk instead. Three patients received the glucose milk mixture given in frequent small feeds for three days and all did well. As long as flavouring with tea or coffee was available the milk was easy to administer and enjoyed by the patients. This is a point of some practical importance. The commonest deficiency present was a pellagra-like lesion of the tongue, gums and buccal mucous membrane, resulting in a sore and dirty mouth. Frequent mouth-washes were out of the question with the scanty nursing help available, and milk alone is apt to become unpleasant under such circumstances. Variation of flavour, however, was greatly appreciated.

¹These figures will need slight correction when the acid used has been standardized. It will not affect their relative value.

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Captain J. A. F. Stevenson, R.C.A.M.C., said that he had been asked to take part in that discussion because of some work with which he had been connected at McGill University, Montreal. At that university for two or three years a study, under the direction of Dr. J. S. L. Browne, had been made of metabolic effects of damage, especially in terms of nitrogen balance. Dr. Cuthbertson as well as workers in Canada and the United States had described the very marked increase in the excretion of nitrogen in the urine following fractures, burns, and similar injuries. During this period of increased protein catabolism it had been the experience of most workers that if the intake of protein by mouth were increased very little alteration in the nitrogen balance resulted. As the intake went up the output went up, so that the nitrogen balance was still negative. It was reported by some workers that they could prevent a negative nitrogen balance by the use of protein hydrolysates given intravenously. It had also been noted that following this period of negative nitrogen balance there was a period in which the excretion of nitrogen decreased. This occurred, say in a case of leg fracture, at about the beginning of the second month after the infliction of the injury, the body excreting less nitrogen than it would do on the same intake in health. It was evidently trying to replace the used-up tissue.

At the McGill University Clinic they had administered protein hydrolysate mixtures in both the earlier period of negative nitrogen balance when protein catabolism was predominant and in the later period when protein anabolism was predominant.

Here the speaker showed and explained a chart illustrating experiments with intravenous Amigen. The patients to whom the chart related had been previously healthy and well fed, but had suffered damage in the shape of fractures. It was indicated on the chart that in such cases the amino-acids given by vein were treated by the body in exactly the same way as food given by mouth. Increasing the nitrogen intake by protein hydrolysates intravenously at the height of the protein catabolic period resulted in an increase in nitrogen excretion and during the protein anabolic period in an increased positive nitrogen balance. Those workers who had found that they could prevent a negative nitrogen balance by using Amigen had been for the most part dealing with cases which previously were in a poor nutritional state. In those people there was very little negative nitrogen balance, following an injury. The lesson from the experiments at McGill was to emphasize the probability that there was very little distinction metabolically so far as the body was concerned between the results of giving amino-acids by vein and food by mouth, which was successfully digested and absorbed. Their great use was where food by mouth could not be successfully digested and absorbed.

Professor R. B. Hawes said that some good might come out of this evil, for hitherto it had been difficult to impress upon responsible persons the gravity of protein shortage in certain parts of the world, and how closely bound up it was with economic life. Everyone could now visualize what the word "starvation" meant. He recalled the first feeding experiment he had ever carried out. It was on a group of labourers, who were taking an inadequate diet of protein, some 20 grammes. When he proposed to increase it to about 70 grammes the objection was made that they were unable to pay for it, but the diet was increased accordingly, and within a month their output also had increased by 50%, and they were able and willing to pay the small extra amount for the increased diet. It had been said that poor people could not pay for adequate protein, but the fact was that they could pay if the protein enabled them to do a proper day's work, which with their low protein intake they had been unable to do.

It was borne out in veterinary science that if the young of an animal were fed on low protein, no matter what was done for them in after-life they would always have lowered resistance to disease. The same appeared to be true in human nutrition. It had been shown by experience that men who in earlier life had had a poor protein intake always succumbed more easily to pneumonia and lung affections, never having the same resistance to disease as others. Whatever was done later in the way of developing their physique and keeping them on an ample and well-balanced diet, that early handicap remained. Perhaps it would convince politicians and others that protein sources must never be thrown away, and that any surplus fish and milk proteins are urgently required in other parts of the globe.

Section of Experimental Medicine and Therapeutics

President—E. N. ALLOTT, F.R.C.P.

[March 13, 1945]

DISCUSSION ON THE FACTORS CONCERNED IN BLOOD COAGULATION AND THEIR CLINICAL SIGNIFICANCE

Dr. R. G. Macfarlane: The study of blood coagulation has been for more than fifty years a sort of academic battlefield for the physiologists. There is something about the obvious yet mysterious conversion of fluid blood into solid clot that has intrigued a curiously large number of workers, many of them of international repute. It is unfortunate, perhaps, that many of them have devised and defended their own theories and terminologies, because the result is a mass of literature that is confusing to subsequent workers. It would also not be unfair to say that, until quite recently, this formidable bulk of experiment, theory, and controversy has contributed very little of practical value to the clinician. A few years ago, in fact, it would have been difficult to find material for a discussion such as this. It was known that abnormalities of the coagulation system might have disastrous consequences for the patient, whether the blood failed to clot when required to, or clotted spontaneously in the vessels. Certain factors concerned in these abnormalities might have been understood, but nothing practical could be done for their prevention. Now, however, this part of the picture has changed, and is still changing rapidly. Academic research is at last bearing the fruit of practical application, saving many lives by such advances as vitamin-K therapy and the use of anti-coagulants in the prevention and treatment of thrombosis.

The function of blood coagulation.—Its most obvious function is the arrest of bleeding. Anyone who has observed the blood clot plugging the socket from which a tooth has just been removed might reasonably suppose that it is this plug that has stopped the bleeding. Moreover, in those conditions in which clotting is delayed or defective, the patient is liable to bleed persistently or even fatally from, or into, any part of the body in which the vessels have been damaged. It is easy, therefore, to suppose rather vaguely that the clotting of blood stops bleeding, and that if the blood fails to clot, bleeding will continue. One cannot, however, explain by this loose hypothesis why persistent bleeding should occur in other conditions such as the purpuras and telangiectasia in which there seems to be nothing wrong with the clotting mechanism. In such cases normal coagulation is incapable of arresting the flow of blood even from a needle puncture. It is probable, therefore, that coagulation is only a part, though an essential part, of a haemostatic system that requires the operation of another factor to be effective. I, personally, believe that it is the active contraction of the damaged vessels, including the capillaries, that is the essential first stage of haemostasis (Macfarlane, 1941). Observations of the reactions of the vessels to trauma in the normal individual and in the haemorrhagic states have suggested the following sequence of events:

- (1) The vessels are severed by trauma, and become dilated by the "H" substance liberated by tissue damage. Blood therefore flows from the wound.
- (2) After a short time (a few minutes in the case of a small superficial wound) the vessels contract and blood ceases to flow. The blood lying in the wound now has time to clot firmly in situ, the clot extending down to the mouths of the torn vessels.
- (3) After a period of contraction lasting 0.5 to two hours, the vessels again dilate, the first step towards repair of the wound. A recurrence of bleeding is now prevented by the preformed blood clot, except in the case of minute injuries with approximated edges such as needle punctures, in which drying of the exudate during capillary contraction appears to be sufficient to maintain haemostasis.

If this view is accepted, it will be seen that abnormal bleeding can be due (a) to a failure of the initial vascular contraction, (b) to a failure of the clotting process, so that a firm clot is not formed in the time available, or (c) to a combination of these defects.

The haemorrhagic tendency of the purpuras and telangiectasia is due to the first defect (deficient vascular contraction) and is limited to those parts of the body in which the

vessels are affected. The "bleeding-time" is prolonged from these vessels, though the coagulation of the blood is normal. In hæmophilia and some cases of fibrinopenia, and hypoprothrombinæmia, the bleeding is due simply to the fact that a clot does not form, or is so friable that it fails to withstand the pressure from the re-dilated blood-vessels. The "bleeding-time" in these states is normal because the capillaries contract normally and there is often a latent period between injury and the onset of persistent bleeding for the same reason. Finally there may be a combination of these two major defects. Such a combination is seen in certain of the rarer hæmorrhagic states, and also in some cases of hypoprothrombinæmia, in which the "bleeding-time" is prolonged, particularly if Ivy's method is used. These views on the part played by the coagulation of the blood in the mechanism of hæmostasis are illustrated diagrammatically in fig. 1.

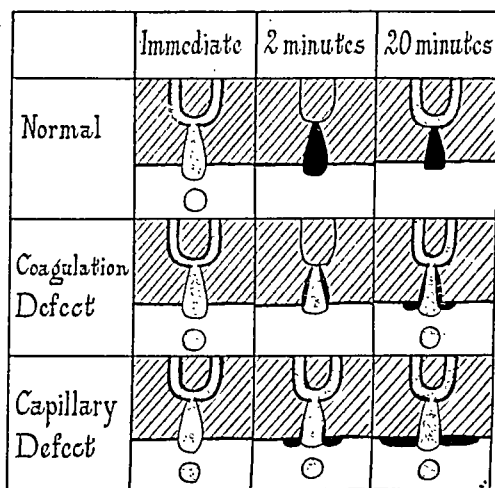


FIG. 1.—Diagram illustrating the time relationships of normal capillary contraction, dilatation and blood coagulation, and the two main defects that may occur. A wound of the skin surface is shown in section, injuring a capillary loop. Fluid blood is represented by the dotted areas, blood-clot by solid black, and the detached "drops" indicate active hæmorrhage.

In addition to its hæmostatic function, coagulation is probably important from other points of view. In the process of repair, for instance, the normal blood clot plugging a cavity provides a useful framework into which the new tissues can grow. In hæmophilia, in which such a framework is not available, there may be a very great delay in the healing of even trivial wounds, so that patients may bleed for weeks from small cuts or abrasions. Secondly, coagulation of fibrinogen in the tissue fluid surrounding an area of infection may help to keep such an infection localized by the formation of a relatively impervious barrier. Lastly, one is impressed by the fact that both fibrinogen and prothrombin disappear rapidly from the blood-stream if, for any reason, their production is prevented. It is possible, therefore, that these two proteins are being consumed by some metabolic process, and that blood coagulation is a particular adaptation of a normally continuous function.

The mechanism of coagulation.—Most theories of coagulation regard the formation of the blood clot as the end-result of a chain of factors reacting one on the other, like the train of wheels in the movement of a watch. Most investigators have sought to take this train of factors to pieces to see how they work separately, and have constructed their own theories as to the natural process by giving the separate parts different names, or by arranging them in different orders. It is true that some of the factors supposed to be concerned with coagulation can be separated, and that they can be reassembled in such a way that coagulation occurs. But like a watch under similar treatment by the amateur, the artificial coagulation mechanism, though it "goes" may not tell the right time. In fact, it is quite possible that some of the familiar components of the accepted theories may be no more than artefacts produced by the manipulation that is required for their separation. It is also possible that the chain-reaction theory of coagulation is wrong in principle, and that it would be more profitable to regard clotting as the result of a physical disturbance of a constantly operating dynamic equilibrium. It is certain, in any case, that the supposedly separate events commonly described overlap in time to a large extent, and that it is the *rate* at which the reactions proceed that determines

coagulation, rather than the total amount of any one factor produced. However, this is no time to complicate the issue by airing yet another theory of coagulation, and for the purposes of this discussion I will base my remarks on a scheme of coagulation that is essentially classical, though simplified as much as possible.

This scheme of coagulation, most of which will be quite familiar, is best discussed with reference to the diagram shown in fig. 2. In this, the factors normally present in the circulating blood-stream are indicated by circles, those that are concerned with the

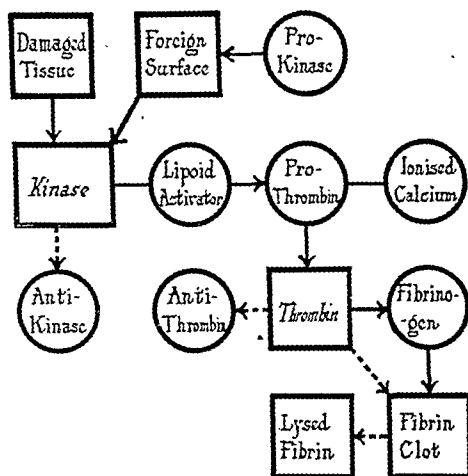


FIG. 2.—The factors supposed to be concerned in coagulation.

inception of coagulation, or appear in the blood only during its progress are shown in squares. The black arrows indicate the direction of coagulation, the dotted arrows the anticoagulant activities. The names in italics indicate that the factors are probably enzymes. These factors will be discussed in the order in which they are supposed to operate.

(1) *Prokinase*.—Since blood taken without any admixture with tissue juice will clot rapidly in contact with a foreign surface, it must be supposed that it contains all the factors required for coagulation. Some of the kinase is probably derived from the platelets, which break up in contact with foreign surfaces in the presence of ionized calcium. But recent work (Lozner^{et al.}, 1942) suggests that kinase is also derived from the cell-free plasma itself, and thus it must be postulated that the circulating blood contains in solution an inactive precursor of kinase, that one can only call "prokinase".

(2) *Foreign surfaces*.—A surface "foreign" in this respect, is one that is wetted by water. Normal blood in contact with normal vascular endothelium does not clot. Normal blood will also remain fluid for considerable periods if it is only in contact with such non-wettable surfaces as paraffin, wax, collodion, or some of the plastic materials. The introduction of a wettable surface such as glass, metal or cotton-wool will result in rapid clotting, though the mode of action of such surfaces in generating kinase is not understood.

(3) *Tissue damage* results in the liberation of cellular debris and tissue fluid which contain large amounts of kinase. The different tissues vary in their kinase content, lung, testis and brain being the richest sources, but most of them are active in this respect.

(4) *Kinase*.—The kinase itself appears to be a water-soluble, enzyme-like factor, the composition of which is unknown. There are reasons for supposing that the venom of Russell's viper is a very powerful kinase. Human saliva contains a similar factor and it is probable that the venom, which is modified saliva, is merely an extreme intensification of a normal salivary constituent.

(5) *The lipoid activator*.—Russell's viper venom will not clot human plasma from which the fat has been removed by high-speed centrifugalization or extraction with carbon tetrachloride. The addition of tissue or plasma lipoid, or lecithin will result in an extremely rapid coagulation by the venom. It can also be shown that the human kinase extracted from tissue or saliva behaves in a similar way. It appears, therefore, that a lipoid is necessary for the action of kinase (Macfarlane *et al.*, 1941).

(6) *Prothrombin*.—The inactive precursor of thrombin is a globulin-like protein, which is normally present in a considerable excess above the amount required for normal coagulation. Vitamin K is needed for its production, and an adequate liver function is necessary for the synthetic process. Vitamin-K deficiency, or severe liver disease may therefore result in a prothrombin deficiency.

(7) *Ionized calcium*.—Calcium in an active state is necessary for the reaction between kinase, the lipoid activator and prothrombin.

(8) *Thrombin*.—Thrombin is released from prothrombin by the action of the factors already mentioned. It has already been stated that there is normally an excess of prothrombin. During the process of coagulation, thrombin is generated and, when its concentration is sufficiently high, it acts on fibrinogen. Thrombin continues to be generated, however, until all the prothrombin is converted, and this may be long after the clotting process is complete. The normal coagulation time, therefore, is dependent, not so much on the total amount of prothrombin, as on the rate at which it is converted by kinase, and this in turn depends on the amount of kinase available. Thus a quite considerable reduction in prothrombin is possible before the blood coagulation time is prolonged. It is only when a very active kinase, such as rabbit brain, or Russell's viper venom, or, most active of all, Russell's viper venom and lecithin is added that the coagulation time (now reduced in normal blood to a few seconds) is influenced by the prothrombin level. This accelerated clotting time is usually called the "prothrombin time".

Fibrinogen.—Fibrinogen is a protein of the plasma with a high molecular weight, and a long fibre-like molecule. Under the influence of thrombin, these molecules agglutinate, so to speak, to form the typical fibres of fibrin, which, entangling the red cells in their meshes, form the familiar blood clot. At first the clot is friable and bulky, but within a few minutes the fibres begin to contract, squeezing out fluid serum so that the clot finally occupies less than half its original volume. It is now much tougher, and better able to withstand the strain of maintaining hæmostasis. Clot retraction is dependent on the platelets, but may be reduced in conditions such as obstructive jaundice, in which the platelets are normal (Macfarlane, 1939).

The anti-coagulant factors.—The primary reason why blood does not normally clot in the vessels is the absence of contact with a water-wettable surface, and the absence, therefore, of a stimulus towards kinase generation. However, trauma, or alterations in the surface of the vascular endothelium, may result in small amounts of kinase being liberated into the general circulation. This small amount is neutralized by an anti-kinase present in the plasma before it can reach a sufficient concentration to act on prothrombin. There is, moreover, an additional factor that inactivates any thrombin which may be produced. This anti-thrombin is probably complex, and is usually regarded as being made up of two factors, the immediate anti-thrombin, and the progressive anti-thrombin. The first may be heparin, which requires a serum protein factor for its action. The second is even less understood, but its effect is well demonstrated by the large amounts of thrombin that are progressively inactivated by normal serum.

By these means coagulation is limited to localized collections of blood, such as in a wound cavity or damaged vessel, in which the rate of production of kinase and thrombin exceeds the rate at which they are neutralized by the anti-enzymes available.

Finally there is a mechanism for disposing of blood clots when their useful purpose has been served. At a varying period after its formation, fibrin disintegrates and goes into solution. This is not a reversion to fibrinogen, since lysed fibrin cannot be made to clot. Fibrinolysis is the result of proteolytic enzymes, some of which are produced by the leucocytes attracted to an injured area. Lysis does, however, occur in cell-free clots in the test tube (Macfarlane, 1937), and the lytic agent can be shown to be associated with thrombin. Some authorities believe that thrombin itself is a proteolytic enzyme, coagulation of fibrinogen being the first stage in its digestion. Others believe that there is a trypsin-like enzyme, distinct, but difficult to separate from thrombin. Fibrinolysis is an interesting phenomenon, and one that has not received its share of attention.

Pathological inhibition of coagulation.—Delayed, or inefficient coagulation may result from a number of different defects in the mechanism, and will produce a generalized hæmorrhagic diathesis.

Hæmophilia is probably the most familiar of these conditions. In this, a sex-linked recessive defect is exhibited by the affected male in the form of a delay in coagulation. Until recently no satisfactory cause for this delay had been discovered. All the factors necessary for coagulation—kinase, lipoid, prothrombin, calcium and fibrinogen—seem to be present in normal amounts, and to be normally active when examined separately. Some authorities considered that the platelets were unduly resistant in this condition, and that their slowness in disintegration led to a deficiency of kinase. There was little to support this view, and more recent work suggests that the platelets, in any case, are not important sources of kinase in the normal process of coagulation. More promising is the finding of Tocantins (1943) that there is an amount of anti-kinase in hæmophilic plasma that is from five to eight times the normal. If this can be confirmed, there will be, at last, a firm basis for research aimed at an effective general treatment for this condition. At present, all that can be done is only symptomatic. No general treatment, with the exception of the transient effect of blood transfusion, has met with any lasting success. Local treatment of accessible bleeding points has been effective in some cases, less so in others. Hæmophilic blood can be clotted in a few seconds by the addition of tissue extracts, or Russell's viper venom—both sources of kinase—and these, particularly the latter, have been used as hæmostatic applications. In this connexion it is important to remember that no coagulant, however quickly it will produce coagulation, can arrest an actual flow of blood. It is always necessary to stop the flow by temporary pressure for a sufficient length of time for the coagulant to produce a clot in the wound area down to the injured vessels. Otherwise the coagulant is simply washed out of the wound to produce clots in a situation in which they are of no use. In many cases, even when a clot is formed in the wound area, it subsequently becomes loosened or dissolved. This is particularly troublesome in the case of infected tooth sockets, and all that can be done is to repeat the application. Thrombin has also been used as a local coagulant, and in the last few years a very active and stable form of thrombin known as "clotting-globulin" has become available (Parfentjev, 1941). Adjuncts to the formation of an effective clot are such active surfaces as cotton-wool or gauze, which not only stimulate coagulation by their large surface area, but also reinforce the substance of the clot, which forms in the interstices of the dressing. Preformed fibrin can also be used most effectively in this way, since, unlike the ordinary dressing, it can be left in situ to be removed by the normal process of repair.

Hypoprothrombinæmia.—Prothrombin deficiency, itself usually the result of vitamin-K deficiency, does not result in a delay in the coagulation of the blood until it is extreme. Patients with a low prothrombin concentration tend to bleed, however, partly because the clots that form are less tough than normal, and partly because there is sometimes an associated capillary defect as demonstrated by a prolonged Ivy "bleeding-time". Such patients, if they lose blood (during an operation for instance), may have a disastrous decrease in their prothrombin level, since the loss of prothrombin by hæmorrhage cannot be made good, and a vicious circle ensues. The treatment in such cases is vitamin-K therapy, transfusion of fresh blood, and, if necessary and possible, the local application of thrombin.

Calcium deficiency.—A deficiency of calcium is usually referred to in the textbooks as a cause of abnormal bleeding. I have never seen such cases, although I have seen patients with hydrocalcæmic tetany. Nevertheless, calcium is still given as a prophylactic in patients expected to bleed, and since it is not likely to do much harm, and it is difficult to prove that it does no good, I suppose it will continue to be given for some time to come.

Fibrinogen deficiency.—A deficiency of fibrinogen may result from very extensive liver destruction, though usually the patient does not survive until this stage is reached. It may also occur as an idiopathic congenital defect, in which case fibrinogen may be completely absent. I have seen two such cases, both the result of first-cousin marriages. The blood, of course, is incoagulable by any means other than the addition of fibrinogen. Nevertheless, the extraordinary thing about these patients is the comparative mildness of the hæmorrhagic symptoms. One of them is a boy, now aged 16, who has led a fairly normal life, having been to school and even played games. He would certainly be classed as a very mild hæmophilic. The other, a girl, is more severely affected, but even she does not show the liability to bleed that one would expect. How these patients stop bleeding after injury I do not know. The boy had thrombocytopenia in addition to his absence of fibrinogen (Macfarlane, 1938).

Excessive fibrinolysis.—Rapid solution of blood clot may be a cause of the so-called secondary hæmorrhage associated with infection. The inflammatory reaction leads to

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Pathological inhibition of coagulation.—Delayed, or inefficient coagulation may result from a number of different defects in the mechanism, and will produce a generalized hæmorrhagic diathesis.

An ingenious application of the coagulation process is that of Dees (1944) who removes multiple stones from the pelvis of the kidney by embedding them in a matrix of fibrin, produced by filling the pelvis with a mixture of fibrinogen and thrombin. The clot, containing all the stones, is then removed in one piece. Thomas, Gough and Still (1943) have reported encouraging results in their attempts to produce collapse of chronic tuberculous pulmonary cavities by occluding the bronchi leading to them by means of a plasma clot produced in situ.

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Dr. Harold Scarborough: The role of prothrombin in the coagulation process has already been described by Dr. Macfarlane. A normal plasma prothrombin depends upon at least two factors—the absorption of fat-soluble vitamin K and adequate hepatic function. Disturbances of vitamin-K metabolism and of hepatic function may therefore both be reflected in low plasma prothrombin levels, in impaired coagulability of the blood and, finally, in a tendency to bleed. The synthesis of prothrombin, in which vitamin K or its synthetic analogues play an indispensable but at present unknown part, is probably confined to the liver and vitamin K even when administered parenterally is not effective in increasing plasma prothrombin and controlling bleeding unless this synthetic process can be accomplished in the liver. The circumstances in which a low plasma prothrombin level and later a manifest bleeding tendency might be expected are best considered in relation to the physiology of vitamin K.

(1) *Dietary intake of vitamin K.*—The daily requirement of man is probably of the order of 1 mg. Patients with frank vitamin-deficiency syndromes very rarely have plasma prothrombin significantly reduced below normal (Scarborough, 1940) and a study of the prothrombin index in 74 cases of scurvy failed to reveal a value below 90% of normal. Probably the main reason for this striking fact is:

(2) *Synthesis of vitamin K* by the intestinal flora, especially by organisms of the coli group (Almquist, Pentler and Mecchi 1938). Although this synthesis is inhibited by sulphonamides the therapeutic administration of these drugs has never been reported as causing a low plasma prothrombin level in man. There is, however, a bleeding disorder in infants in which defective bacterial synthesis probably plays a major role. The importance of neonatal bleeding has been emphasized by Brenneman who stated that 25-40% of neonatal deaths could be attributed to intracranial hæmorrhage and by Roberts who estimated that the latter occurred in 2% of all infants. It is now well established that this condition is due to impaired blood coagulability as the result of a low plasma prothrombin but the mechanism by which this is produced is not so clear. In apparently healthy, but especially in premature, infants at birth there may be observed a deficiency of plasma prothrombin which tends to fall during the subsequent two to six days. The facts that (a) administration of vitamin K to the mother can increase the prothrombin in the infant's blood and (b) that maternal toxæmia is frequently attended by low plasma prothrombin levels in the infant suggest that an impaired maternal contribution of vitamin may play a part. Other factors which may be important in specific cases are, for example, defective synthesis of prothrombin by the infant's liver, defective secretion of bile and limited absorption of fat, gastro-intestinal hypermotility and a low content of vitamin K in the milk. Neonatal bleeding due to hypoprothrombinæmia is controlled by the administration of a synthetic vitamin-K analogue given parenterally in a dose of 2 mg. of a water-soluble derivative or as an injection containing 10 mg. of a fat-soluble compound. It is not as a rule necessary to repeat the dose. The indications for such treatment have been summarized by Macpherson (1940). They are (a) maternal toxæmia,

the accumulation of leucocytes, which release proteolytic enzymes that digest any fibrin in the vicinity. Clots plugging wounded vessels may therefore give way, with consequent hæmorrhage. There is a rare condition known as "purpura thrombolytica" (Reimann, 1941) in which the fibrinolytic power of the serum is greatly increased, so that clots may be lysed almost as soon as they are formed, and a generalized hæmorrhagic tendency result.

Intravascular coagulation.—Clotting of blood in injured vessels is, of course, a normal part of the hæmostatic mechanism. In certain cases of tissue damage, however, this process exceeds its normal limits, so that clotting may extend into undamaged vessels whose patency is necessary for the maintenance of the blood supply of a large or important area, or clotting may even occur in normal vessels in a different part of the body altogether. Such thrombosis may arise in vessels in which the endothelium has been changed by inflammation, or destroyed by atheroma or infection. It is clear that some people seem to be more susceptible to this danger than others, though no satisfactory explanation has yet been produced. The ordinary methods of examining the coagulation mechanism do not reveal any obvious abnormality. The essential factors involved in this abnormal extension of the natural process seem to be these:

(a) The rate and amount of kinase liberated into the vascular bed concerned. This, of course, depends on the extent and nature of any trauma or inflammation, and on the condition of the vascular endothelium.

(b) Stasis of the blood into which kinase is liberated. Large amounts of kinase can be injected into the normal circulation without producing intravascular clotting. By being mixed with a large volume of blood, the kinase is brought into contact with a large amount of anti-kinase and anti-thrombin, and it is neutralized before its concentration at any one point can rise to the level required for clotting. In the cases of static or sluggishly-flowing blood, however, the kinase content may rise locally and overpower the comparatively small amount of the anti-coagulant factors available.

(c) The general concentration of anti-kinase and anti-thrombin. These factors have not yet been quantitatively studied on a large scale, but it is possible that such a study might throw light on the otherwise puzzling incidence of thrombosis and embolism.

The use of heparin in the treatment and prevention of these conditions has been of very great benefit. In fact, the danger of post-operative thrombosis and embolism may well be overcome altogether by a judicious increase of the general anti-thrombin concentration. In vascular surgery, operations that would otherwise have been impossible are being carried out on battle casualties with the help of heparinization. Dicoumarin also has been claimed as an anti-coagulant of considerable use, but its action is more complicated, more uncertain, and not without danger. Natural heparin, or possibly synthetic substances with a similar action, would seem to be the most promising agents for this type of therapy.

Finally I come to the interesting and practical use of preformed human fibrin as a hæmostatic, as a physiological filling for traumatic or surgical cavities, and as a covering for raw areas. In 1941 I used sheets or membranes of elastic human fibrin as a dressing for burns. The membranes were made by clotting human plasma in the shallow dishes used for developing photographic films, and then washing the thin sheets of clot free from serum, and pressing them between layers of filter paper. The membranes were attached to the raw surface with recalcified plasma or with fibrinogen and thrombin. In one or two cases (Macfarlane, 1943) these membranes were successful, but in most there was a tendency for them to lyse before healing was complete, or for the burn to become infected. More promising was the use of small bits of these membranes, stuck like postage stamps, after soaking in thrombin, on to the bleeding points in tooth sockets or traumatic injuries in hæmophiles.

American workers have succeeded in improving the physical properties of preformed human fibrin. They have produced a series of "plasticized" products, in which the permeability and liability to lysis have been reduced (Ferry and Morrison, 1944). These products have been used as a dressing for burns (Hawn, *et al.*, 1944), as a hæmostatic agent (Bering, 1944), as a filling for the cavities left after the removal of cerebral tumours and as a dural substitute in neurosurgery (Bailey and Ingraham, 1944). The great advantage of these products is that being a physiological substance fibrin can be left *in situ* to be removed by the ordinary process of healing and repair. There is no danger, therefore, of re-starting bleeding as is so often the case when artificial hæmostatic packing has finally to be removed.

While neither the plasma prothrombin level nor the prothrombin response to K injection can at present be regarded as very useful tests of hepatic function it is possible that further work may explain certain anomalies. It has, for example, been found in 15 cases of hepatitis that the subjects with the higher levels of plasma vitamin A were those in which the plasma prothrombin rose normally following an injection of 10 mg. of a water-soluble vitamin-K analogue. Those with plasma vitamin A below about 150 i.u. per 100 ml. did not respond (fig. 1). This finding cannot be explained on the

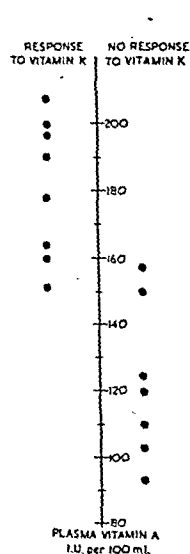


FIG. 1.

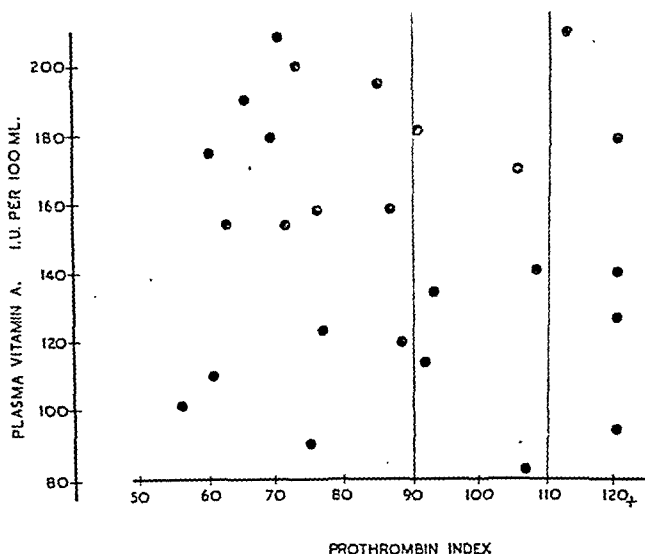


FIG. 2.

24 cases of hepatitis (23 observations).

basis that the latter group contained the more severe cases since in 24 cases of hepatitis (fig. 2) there was no correlation between the plasma prothrombin (expressed as an index) and the plasma vitamin A.

The synthesis of prothrombin by the liver, or possibly the participation of prothrombin in the coagulation process, is inhibited by dicoumarin, the active principle of spoiled sweet clover hay isolated by Link and his associates in 1939 and now available in synthetic form as an *in vivo* anti-coagulant. Dicoumarin has recently been introduced for the treatment of thrombophlebitis, post-operative thrombosis and embolism, threatened gangrene and thrombo-angiitis with a view to preventing extension or recurrence of thrombosis, reducing the incidence of secondary embolism, and shortening the period of stay in hospital. Although it has been reported upon favourably (Lehman, 1943; Barker, Allen and Waugh, 1943) it cannot be said that its therapeutic value has been clearly established. Pulmonary emboli have occurred during treatment and relapses have been reported following withdrawal. It is contra-indicated in cardiac or hepatic disorder, with severe arteriosclerosis, in hypertension and nephritis and in pregnancy and the puerperium. Dicoumarin is a toxic drug, whose absorption is probably irregular and to the effects of which there may be wide individual variation. These effects, apart from an increase in the prothrombin time and delayed coagulation, include an impaired clot retraction and increased sedimentation rate and bleeding time, capillary dilatation and decreased capillary resistance. It is said to decrease clot firmness and clot resistance in animals (Lalich and Copley, 1942, 1943). The drug has a prolonged action so that its effect upon the prothrombin time may outlast its administration for seven to fourteen days and there is a latent period of two to four days before it becomes effective when given by mouth. Its administration requires careful control by daily estimations of the prothrombin time which should not be allowed to fall below 60% of normal. Even so, unpredictable hemorrhage, often from the rectum and into the urinary tract, may occur during treatment and this bleeding is most difficult to control except temporarily by transfusions of fresh blood. Recently,

(b) premature labour, (c) difficult instrumental delivery, (d) when breast feeding is impossible, (e) if cerebral signs are present in the first few days of life, (f) if a hæmorrhagic diathesis is manifest, and in icterus gravis neonatorum and so-called congenital anemia, (g) if surgical operation is necessary. It has been established that hypoprothrombinæmia in the infant can be prevented by giving vitamin K to the mother. Since, however, a dangerously low prothrombin in the infant may occur with a normal maternal prothrombin no pre-selection of cases for treatment is possible and vitamin K should therefore be given to all mothers at, or shortly before, labour. In spite of the demonstration by many workers that the incidence of hypoprothrombinæmia, neonatal hæmorrhage and possibly intracranial hæmorrhage can thereby be greatly reduced this is not yet the routine practice in this country.

(3) *Absorption of vitamin K* from the intestine like that of other fat-soluble vitamins depends upon bile salt and therefore may be defective in obstructive jaundice and with biliary fistulæ. Administration of bile salt in keratin-coated capsules will correct hypoprothrombinæmia due to this cause. Zuckerman (1939) has reported a case in which the prothrombin fell to 33% of normal and bleeding occurred within fourteen days of a biliary fistula having been performed. However, such rapid falls are unusual both in animals and in man.

Hypoprothrombinæmia follows steatorrhœa and the taking of liquid paraffin over long periods. It is corrected by injection of K analogue. The prothrombin gradually increases spontaneously as absorption improves.

(4) *Disturbed intestinal motility* is a potent cause of hypoprothrombinæmia probably because it occasions anomalies of absorption. Intestinal anastomosis, enterostomy, fistulæ, obstruction, pyloric stenosis, ileus, continuous gastric suction and long-continued diarrhœa and vomiting may lead fairly rapidly to low plasma prothrombin levels and treatment by injection is often a matter of some urgency.

(5) *Following surgical operation* in patients with obstructive jaundice and parenchymal liver disorder the plasma prothrombin may fall rapidly but a normal prothrombin before operation is no guarantee that post-operative bleeding will not occur from hypoprothrombinæmia. Although the fall may occur within a few hours or be delayed as long as eighteen days, the bleeding usually occurs within three to five days after operation. While it may be true that there is a greater utilization of prothrombin and, therefore, an increased requirement for vitamin K, following operation more important factors are probably an impaired prothrombin synthesis in the liver, a diet temporarily deficient in vitamin K, disturbed intestinal motility and defective absorption. The condition is resolved by injection of K analogue in doses of 10 mg. on each of three successive days. It may be prevented by the same method.

(6) *Synthesis of prothrombin in the liver.*—The key-role that the liver plays in the synthesis of prothrombin has suggested (a) that low plasma prothrombin levels might be found in hepatic disease and might serve as an index of hepatic function, and (b) that the response of the plasma prothrombin to an injection of vitamin K might serve as an hepatic efficiency test. However, in man the striking falls of plasma prothrombin which are found in animals after experimental liver damage (see Rhoads, Warren and Panzer, 1941) are rarely found. In acute liver disorder the plasma prothrombin level is remarkably well maintained even to death. In chronic liver disease on the other hand, a progressive and gradual fall in plasma prothrombin can often be noted which, however, is usually preceded by a fall in the plasma albumin. Low prothrombin levels are irregularly found in liver disease and they bear no constant relation to the type of hepatic or biliary disease present. Very low values are rare and it is unusual to find the prothrombin reduced to a level at which bleeding might occur (20 to 30% of normal). It is clear that hypoprothrombinæmia is not the sole cause of a bleeding tendency in liver disease.

Liver damage or the administration of dicoumarin or salicylate are, so far as we know, the only circumstances in which injection of vitamin K will not restore to normal a low plasma prothrombin. The failure of a low plasma prothrombin to rise within twenty-four hours of the injection of 10 mg. of a vitamin-K analogue therefore usually means liver disease. Although even a severely damaged liver is capable of synthesizing prothrombin adequately, Sweet, Lucia and Aggeler (1942) have suggested that the prothrombin level is a more accurate index of parenchymal hepatic tissue destruction than of impaired function.

Section of the History of Medicine

President—Sir ARTHUR MACNALT, K.C.B., M.D.

[February 7, 1945]

Auenbrugger and Laennec: The Discoverers of Percussion and Auscultation

By Professor S. LYLE CUMMINS, C.B., C.M.G.

HISTORY often throws a light on present-day methods in medicine and a fresh study of the works of Auenbrugger and of Laennec as well as of their comrades and their opponents appears appropriate.

LEOPOLD AUENBRUGGER (1722-1809).

It seems proper that I should put Auenbrugger first among the Continental phthisiologists, although he was never very celebrated for a study of phthisis, for he introduced what has proved to be one of the most fruitful methods for investigating diseases of the chest—percussion.

As the son of an inn-keeper father and a musical mother, he had the right physical make-up for the differentiation of sounds and must, as has often been pointed out, have seen his father investigating the amount of fluid in barrels by tapping their sides; he was suitably endowed, therefore, to appreciate the advantages of examining the human chest by percussion.

With the passage of more than seventeen centuries of the Christian Era, doctors then still left the chests of their patients unexamined and depended upon cough, fever and wasting to indicate disease. It was reserved for Auenbrugger to discover percussion. From Graz, where he had been born, he was launched by his father on the study of medicine and soon became a well-known figure in Vienna. He was a student under Van Swieten, the celebrated Professor of Medicine who had been attracted from Leyden to the Vienna school. He became a physician to the Spanish Military Hospital and continued there for ten years, for the last seven of which he devoted himself to the study of chest percussion. He published his *Inventum Novum* in 1761 when he gave up his connexion with the hospital.

"In making public my discoveries respecting the matter" he writes, "I have been actuated neither by an itch for writing nor a fondness for speculation but by the desire of submitting to my brethren the fruits of seven years' observation and reflection. In doing so I have not been unconscious of the dangers I must encounter since it has always been the fate of those who have illustrated or improved the Arts and Sciences by their discoveries to be beset by envy, hatred, malice, detraction and calumny."

He was right. Though popular as a man and taken into favour by the Court and the Empress Marie Thérèse, his *Inventum Novum* remained unnoticed by those great physicians and professors, Baron van Swieten and his successor, de Haen. There must have been some temporary professional interest in the matter for the little book went through two editions; Stoll, the successor to de Haen, rather favoured it and Albrecht von Haller thought the technique "worthy of close attention". Though quickly forgotten in Vienna and the surrounding countries, the *Inventum Novum* caught the attention of Rosière de la Chassagne of Montpellier in 1770 though this observer merely regarded it as "un moyen de plus qu'on peut employer sans risque", never tried it himself and confounded it with the Hippocratic succussion from which, needless to say, it differs completely. From that time percussion seems to have been completely ignored until it was found by Corvisart to be mentioned in the *Aphorisms* of Stoll and was republished by him with weighty additions in 1808. The volume by Corvisart, 439 pages as compared with the original 74 pages of Auenbrugger, consists of an elaborate analysis of the Sections of the *Inventum Novum*. It finally made the method widely known and gave it its place as a really valuable technique to be followed in the examination of the chest. Above all, it came to the notice of Corvisart's great pupil, Laennec, and thus ensured its combination with mediate auscultation as a very promising procedure.

Up to the time of Corvisart, and for several years after, percussion meant the simple tapping of the chest with the flexed fingers worked from the wrist, not from the elbow or shoulder. In 1827-28, Pierre Adolphe Piorry introduced the method of "percussion médiate", the use of a pleximeter; that finally preferred by him was a plate of ivory, to be held against the chest with a bent handle. He tapped upon this with the finger.

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In view of the dangers which attend its use it is considered that dicoumarin treatment is justifiable only if close observation and control are possible; it is not suitable for general use in the prophylaxis of post-operative thrombosis and embolism. A useful review of the place of dicoumarin and heparin in therapeutics is available (Pfeiffer and Sain, 1944).

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My suggestion is that before every operation the patient's blood should be examined to see whether its fibrin is not too weak, and if it is, an attempt should be made to combat the weakness either by administering calcium phosphate or by subcutaneous injection of calcium-glycerin-phosphate.

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case of the big, managing Dupuytren against the little, but determined, Laennec, and Dupuytren tried to drub his small adversary in subsequent correspondence and controversies—but it is remarkable how successfully Laennec came through the storm. He may have been a little bit injudicious but, at least, Dupuytren afterwards was the first to hold out the hand of friendship to him and Laennec grasped it firmly. It is remarkable how, even as a student, Laennec managed to write and publish the most stimulating researches. Perhaps his most remarkable work, at this time, was his *Histoire Anatomique et Clinique des péritonites Aiguës*, written in 1802. This was concerned with practically a new discovery or at least dealt with the subject from a new angle. It was very widely discussed and was greatly admired for its clearness as well as for its novelty. He sat for his examinations in 1803 and got two prizes, one in Practical Medicine and the other in Surgery. In 1804 he became a doctor. A few months later he published his *Thesis on Hippocrates in Latin* and a second thesis *Propositions sur la Doctrine d'Hippocrate relativement à la Médecine Pratique*, in French. He made valuable contributions to our knowledge of the fibrous sheaths of the viscera and to the study of the musculature of the prostate; and, in helminthology, published his *Mémoire sur les vers vésiculaires*. In other words, he was already a skilled morbid anatomist as well as a general research student both after and even before he was qualified! And, for the twelve years after his admission to the medical profession, he added to his growing reputation, finally becoming a physician to the Necker Hospital. But we must hurry on to the work for which he will ever be most famous; his work on mediate auscultation. He, like others, had felt the necessity to understand better the processes by which the tubercles which he had observed, and which he had so well described, and the many other diseases of the chest studied by him in the post-mortem room, might be followed up during life and, in some cases, perhaps, arrested or cured. Let us first consider the attitude to tuberculosis current at the time. As Roxeau says: "One lived as well as one could on the little that was known of the work of William Stark, unhappily interrupted too soon by the premature death of this young savant". As a matter of fact William Stark had written his description of tubercles and their breaking down into vomicae, the relative loss of vascularity around them by the sealing off of the vessels and the opening into them of bronchi and bronchioli which had likewise been interrupted in their course by the tuberculous process, nearly twenty years before the birth of Laennec; but he had written of them very briefly though very thoroughly and his work owing to his sudden death had remained unpublished until 1782. One imagines that this work was only slightly known and appreciated by the profession in France as, indeed, it was equally unread in the England of that time. But it was not altogether ignored and it probably served as the inspiration of men like Bayle and Laennec. Bayle had already published his 900 cases of phthisis due to respiratory disorders and had declared at least 624 of them to be tuberculous in origin. Laennec had gone further, had recognized the tuberculous nature of the *phthisis granulæuse*, which Bayle had understood to be a separate development, had stated his belief that the 183 cases of this kind should be added to the total of tuberculosis described by Bayle; and had thus put the crowning touch to his studies of this disease by announcing the unity of the various manifestations of tuberculosis under this one heading. Now it remained to him to discover a means by which all these tuberculous signs, as well as many others, non-tuberculous, affecting the lungs and the heart, might be recognized during the life of the patient. One day, walking across the court of the Louvre, he noticed some children with their ears placed to the extremities of long pieces of wood which transmitted the sound of little blows—scratches—struck at the opposite ends. "Cette expérience vulgaire d'acoustie" was an inspiration to him. He at once conceived the idea of applying it to the study of heart maladies. On the morrow, at his clinic at the Necker Hospital, he took the visit card, rolled it up on itself, tied it tight so as to make a central canal, and placed it over the heart of a patient. Such was the account given by Laennec himself to Lejumeau de Kergaradec, a friend of his.

It is as well, I think, to quote Laennec's own words on this discovery as translated by John Forbes who, like James Clark, was one of those who made known the method in England:

"In 1816, I was consulted by a young woman labouring under the general symptoms of diseased heart and in whose case percussion and the application of the hand were of little avail on account of the great degree of fatness. The other method just mentioned (immediate auscultation) being rendered inadmissible by the age and sex of the patient, I happened to recollect a simple and well known fact in acoustics and fancied it might be turned to some use on the present occasion. The fact I allude to is the great distinctness with which we hear the scratch of a pin at one end of a piece of wood on applying our ear to the other. Immediately, on this suggestion, I rolled a quire of paper

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Auenbrugger's percussion technique but it was in reality a valuable extension of it and deserves to be particularly noted, especially the modification of it with the finger as a pleximeter. There is, I think, a sensation to be gained with the finger-pleximeter which lends a definite precision to the method; a sensation which tends to be lost with the ivory instrument. This, however, is an individual opinion and must be taken as such.

But above all there remains the wonderful observation of Auenbrugger that the thorax, on being tapped, has, even in health, several voices and that these may be further modified in disease. "I here present the reader", he says, "with a new sign which I have discovered for detecting diseases of the chest".

"What I have written", says Auenbrugger, "I have proved again and again by the testimony of my own senses and amid laborious and tedious exertions; still guarding, on all occasions, against the seductive influence of self love."

Before bidding adieu to Edler von Auenbrugg—he was ennobled in 1784—it is but fitting to revert to Corvisart for a moment; nor is this a bad method of introducing Laennec, for Corvisart was the teacher and friend of that great man.

Corvisart, that wild student of the Law, who frequented the Quartier Latin and the Medical Schools and, at last, greatly to his father's disgust, abandoned his legal studies and took to medicine as his natural mode of self-expression; who finally won the confidence and regard of Napoleon; who was a Professor of Medicine at the Charité and became Baron Corvisart and Physician to the Court—surely this man, as the discoverer of the outstanding merit of Auenbrugger and the teacher of Laennec, deserves to have his memory cherished by every student of medicine.

Then, too, before we turn to Laennec's own history, there is another to be considered, Gaspard Laurent Bayle, whose researches on pulmonary phthisis (1810) make such a valuable addition to the works of Laennec.

Dupuytren, Bichat and Louis are others whose memory should be recalled as helping on the great work now to be considered.

RÉNÉ THÉOPHILE HYACINTHE LAENNEC (1781-1826).

It seems to me that I should be "bringing coals to Newcastle" if I attempted to describe to this learned assembly the childhood of Laennec or his ancestry which have been so well set forth by Roxeau and so well done into English by Hale-White and others. It would even be superfluous to attempt to describe, except in brief, the original models of the stethoscope which must be known by all admirers of the great inventor. It will suffice to say that Laennec was born at Quimper, in Brittany, on February 16, 1781; that, after his mother's death, his father, a not very satisfactory man for the bringing up of children, gave him over to the care of his brother, a priest, who was afterwards obliged to flee the country owing to the general proscription of the clergy; that he then became the ward of another of his father's brothers, Dr. Guillaume François Laennec, of Nantes; and that, under the guidance of this excellent man, he determined to enter the medical profession; became a military surgeon of the third class at Nantes at the age of 15 and without a medical qualification rose to be an Officier de Santé in 1800 and went with the military expedition to quell the insurrection in the Morbihan district between Nantes and Quimper; left Nantes for Paris and started his medical studies there in that year. From that time on until his death he was a devoted student of medicine. As Hale-White says: "His genius began to unfold; he exulted in his profession". In spite of occasional bad health he must have been, at that time, though small and spare, a fine high-spirited youth, very much attached to a country life and to shooting and other country sports but compelled, as so many of us are in this crowded age, to turn his back on them and devote himself to study; and study very hard he did, to find a place for himself in the crowded life of Paris! He placed himself under Corvisart at the Charité and, inspired by Bichat's work, took up morbid anatomy as his main interest for the moment. In morbid anatomy he seems to have struck a subject with a wonderful interest for him and he became associated with Bayle, a slightly older man than himself, and with Dupuytren, a surgeon pursuing the study of the same kind of material that he was following, and destined to become later, Baron Dupuytren, surgeon to Napoleon and his Court. Dupuytren, Bayle and Laennec! What a trio! And all under the influence of Bichat, one of the most celebrated morbid anatomists of his day! It is not to be wondered at that they began to obtain results of surpassing importance. Bichat, however, died in 1803 and Dupuytren, unfortunately for the trio of workers, produced, though I think he did not publish, a *Traité d'Anatomie Pathologique* in that year; a *Traité* which struck Laennec as containing ideas, as he said, "un peu de chose près celles de Bichat". Laennec resented as plagiarism this approach by another to the most intimate ideas of the Master and he also resented the use of a classification of diseases which he himself had set forth in priority in a course of lectures given a few months before. He now adverted to this classification in the course of a lecture at which Dupuytren was present. It was a

case of the big, managing Dupuytren against the little, but determined, Laennec, and Dupuytren tried to drub his small adversary in subsequent correspondence and controversies—but it is remarkable how successfully Laennec came through the storm. He may have been a little bit injudicious but, at least, Dupuytren afterwards was the first to hold out the hand of friendship to him and Laennec grasped it firmly. It is remarkable how, even as a student, Laennec managed to write and publish the most stimulating researches. Perhaps his most remarkable work, at this time, was his *Histoire Anatomique et Clinique des péritonites Aiguës*, written in 1802. This was concerned with practically a new discovery or at least dealt with the subject from a new angle. It was very widely discussed and was greatly admired for its clearness as well as for its novelty. He sat for his examinations in 1803 and got two prizes, one in Practical Medicine and the other in Surgery. In 1804 he became a doctor. A few months later he published his *Thesis on Hippocrates* in Latin and a second thesis *Propositions sur la Doctrine d'Hippocrate relativement à la Médecine Pratique*, in French. He made valuable contributions to our knowledge of the fibrous sheaths of the viscera and to the study of the musculature of the prostate; and, in helminthology, published his *Mémoire sur les vers vésiculaires*. In other words, he was already a skilled morbid anatomist as well as a general research student both after and even before he was qualified! And, for the twelve years after his admission to the medical profession, he added to his growing reputation, finally becoming a physician to the Necker Hospital. But we must hurry on to the work for which he will ever be most famous; his work on mediate auscultation. He, like others, had felt the necessity to understand better the processes by which the tubercles which he had observed, and which he had so well described, and the many other diseases of the chest studied by him in the post-mortem room, might be followed up during life and, in some cases, perhaps, arrested or cured. Let us first consider the attitude to tuberculosis current at the time. As Roxeau says: "One lived as well as one could on the little that was known of the work of William Stark, unhappily interrupted too soon by the premature death of this young savant". As a matter of fact William Stark had written his description of tubercles and their breaking down into vomicae, the relative loss of vascularity around them by the sealing off of the vessels and the opening into them of bronchi and bronchioli which had likewise been interrupted in their course by the tuberculous process, nearly twenty years before the birth of Laennec; but he had written of them very briefly though very thoroughly and his work owing to his sudden death had remained unpublished until 1782. One imagines that this work was only slightly known and appreciated by the profession in France as, indeed, it was equally unread in the England of that time. But it was not altogether ignored and it probably served as the inspiration of men like Bayle and Laennec. Bayle had already published his 900 cases of phthisis due to respiratory disorders and had declared at least 624 of them to be tuberculous in origin. Laennec had gone further, had recognized the tuberculous nature of the *phthisis granuleuse*, which Bayle had understood to be a separate development, had stated his belief that the 183 cases of this kind should be added to the total of tuberculosis described by Bayle; and had thus put the crowning touch to his studies of this disease by announcing the unity of the various manifestations of tuberculosis under this one heading. Now it remained to him to discover a means by which all these tuberculous signs, as well as many others, non-tuberculous, affecting the lungs and the heart, might be recognized during the life of the patient. One day, walking across the court of the Louvre, he noticed some children with their ears placed to the extremities of long pieces of wood which transmitted the sound of little blows—scratches—struck at the opposite ends. "Cette expérience vulgaire d'acoustie" was an inspiration to him. He at once conceived the idea of applying it to the study of heart maladies. On the morrow, at his clinic at the Necker Hospital, he took the visit card, rolled it up on itself, tied it tight so as to make a central canal, and placed it over the heart of a patient. Such was the account given by Laennec himself to Lejumeau de Kergaradec, a friend of his.

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into a kind of cylinder and applied one end of it to the region of the heart and the other to my ear and was not a little surprised and pleased to find that I could thereby perceive the action of the heart in a manner much more clear and distinct than I had ever been able to do by the immediate application of the ear. From that moment I imagined that the circumstance might furnish means for enabling us to ascertain the character not only of the action of the heart but of every species of sound produced by the motion of all the thoracic viscera."

Auscultation had been discovered. Laennec soon began to find types of cylinder or stethoscope, as he called his tube, more fitting than his paper roll. "Bodies of a moderate density such as paper, the lighter kinds of wood or Indian cane, are those which I have always found preferable to others." But he pauses: "The employment of this new method must not make us forget that of Auenbrugger. On the contrary the latter acquires quite a fresh degree of value through the simultaneous employment of the former and becomes applicable in many cases wherein its solitary employment is either useless or hurtful." There we have it at last: *the linking up of two wonderful discoveries of two men of genius—Auenbrugger and Laennec!*

Laennec lost no time in gathering the honey from his great collection of flowers; the numbers of cases of all kinds that were at his disposal. He may be quoted again, though most of you are probably well acquainted with the passage, in connexion with the auscultation of the voice:

"In the very earliest period of my researches on mediate auscultation I attempted to ascertain the differences which the sound of the voice within the chest might occasion. In examining several subjects with this view I was struck with the discovery of a very singular phenomenon. In the case of a woman affected with a slight bilious fever and a recent cough, having the character of a pulmonary catarrh, on applying the cylinder below the middle of the right clavicle while she was speaking, her voice seemed to come directly from the chest and to reach the ear through the central canal of the instrument. This peculiar phenomenon was confined to a space about an inch square and was not discoverable in any other part of the chest. Being ignorant of the cause of this singularity I examined, with a view to its elucidation, the greater number of patients in the Hospital and I found it in about twenty. . . . The subsequent death in the Hospital of the greater number of individuals who had exhibited this phenomenon enabled me to ascertain the correctness of my supposition; in every case I found excavations in the lungs of various sizes, the consequence of the dissolution of tubercles, and all communicating with the bronchia by openings of different diameters. . . . This circumstance naturally led me to think that *pectoriloquism* is occasioned by the superior vibration produced by the voice in parts having a more solid and wider extent of surface, and I imagined that, if this were so, the same effect ought to result from the application of the cylinder to the larynx and trachea of a person in health. My conjecture proved correct."

I cannot refrain from quoting to you this remarkable example of Laennec's research methods but I shall say no more about them as you already know all that is to be known about mediate auscultation. Suffice it to say that he laid down a system of stethoscopy and described, in an enduring way, the various types of sound to be heard over the normal and the abnormal chest: vesicular breathing, bronchial breathing, diminished breathing; the modifications of the voice as, for instance, pectoriloquy; and the sounds on the production of fluid alone, air and fluid, &c., as *egophony*; and all this with a careful application of percussion to supplement the stethoscope. It is a wonderful record; and, taken with his morbid anatomy findings, the demonstration of the "unity" of tuberculous lesions, the discovery of "dilatation of the bronchi"—"bronchiectasis" as we should call it—the profound study of emphysema of the lungs, and the numerous non-pulmonary observations on peritonitis, brain tumours, worms, &c., it constitutes an almost incredible amount of original work crowded into one short life. For Laennec was to die young. It seems probable that both he and Bayle contracted the tuberculosis that killed them from their long and arduous observations at the post-mortem table; nothing was then known of the infectious nature of tuberculosis nor of the necessity for sterilization of hands, instruments, &c., and yet Laennec speaks of having carried out at least 200 autopsies on pulmonary tuberculous cases alone!

It is necessary for me, however, to remember that this is not a life of Laennec; it is so tempting to deal with him as if it were; but I must hurry on. His heart was always in Kerlouarnec, where the sea air had often brought him back to health; where there was shooting and sport to be had; where there was peace from the jealousies and misunderstandings of his professional brethren! And he himself was there from time to time; once for a period of broken health of nearly two years. He was a Professor of Medicine and held clinics at the Charité from 1823. In 1824 he was married, not in a spirit of romance but rather, from his point of view, for the sake of quiet and a home and, for hers, freedom from the scandal that might arise if she were merely to live with him and take care of him. She was his relative, Madame Argou. The marriage proved a great success. He died on August 13, 1826, at Kerlouarnec, the Place of Foxes; the beloved place where he had passed the happiest days of his life.

Section of Otology

President—L. GRAHAM BROWN, F.R.C.S.

[November 3, 1944]

Conclusions Based on Twenty-Five Years' Practice in Mastoid Surgery

PRESIDENT'S ADDRESS

By L. GRAHAM BROWN, F.R.C.S.

To attempt a review of mastoid surgery during the past quarter of a century would be beyond the scope of this Address. It may prove useful if I express some thoughts upon the subject of mastoid surgery which are the outcome of my own experience.

I believe the opportunities for mastoid surgery are gradually decreasing in proportion as the prophylactic measures against the incidence and spread of aural disease increase. Indeed, the time may not be far distant when intracranial complications of otitic origin will be considered rare phenomena.

During my apprenticeship I can well remember having been greatly shocked by the gross infection occurring in post-operative mastoid wounds. It was a time when the method of packing the open wound was still in vogue. There resulted too many a failure in the form of chronic middle-ear suppuration, post-auricular fistulæ or unsightly scars and depressions. Even keloids of the scar tissue were not uncommon. Mollison (1937) has recorded the advance in theory and practice which has helped in bringing about the better results to-day. This improvement has been obtained mainly by three important factors, viz. the position of the skin incision, the technique of operation upon the soft tissues and diseased bone, and the post-operative care of the wound.

The essential points are: The skin incision, instead of being in or near the post-auricular sulcus, should curve widely outwards, even to the hair-line, and thus provide a large anterior skin-flap which on replacement will entirely cover the bony cavity. There should be as little interference as possible with the soft tissues. That is to say, the temporal muscle should not be incised, whilst the periosteum should be dealt with by a T-shaped incision and carefully preserved by elevating it from the small area of bony cortex which later has to be removed. There should be little if any interference with the attachment of the sterno-cleido-mastoid muscle to the mastoid process, and the latter, likewise, should be preserved as far as possible. There should be a thorough removal of all diseased bony and cellular structures by means of gouge and curette, whilst the cavity remaining should be smooth and shelving. The wound should be completely closed except to provide drainage at the lower end by means of a small rubber tube. Finally, meticulous post-operative attention should be given to the wound. The latter, if it cannot be undertaken by the surgeon himself, should be left only to a carefully trained assistant, preferably, in hospital, the ward-Sister.

Syringing the wound cavity and the external auditory meatus is an infinitely better method of cleansing the ear than swabbing with pieces of cotton-wool. The latter can be not only a painful procedure but can cause delay in healing owing to irritation of the repair granulation tissue. To help to get rid of the initial infection, and to prevent reinfection of the wound and middle-ear cavity, I strongly advocate the use of 50 to 60% of S.V.R. applied on a strip of $\frac{1}{4}$ in. ribbon gauze. Following these essentials, the average time of complete closure of the wound and healing of the tympanic membrane should be no more than twelve days. From time to time there have been advocates for the complete closure of the mastoid wound at the time of operation; recently the advent of the sulphonamides and their use in powdered form may bring about this desired gain.

For the radical mastoidectomy the same essentials should apply, except that the posterior wound can be completely closed, drainage being provided for through a flap in the external auditory canal. Here arises a debatable point. To what extent should a plastic flap be cut in the meatal wall? I have long been an advocate of using the smallest one possible. Unlike Körner, Panse, Ballance and others, I never invade the cartilaginous portion. Such a procedure should be reserved only for cases of cicatricial stenosis of the canal, very often the results of previous bad surgery. I content myself with a small tongue-shaped flap which is really the extremity of the posterior membranous portion. Such a small flap tends to decrease the eventual size of the healed cavity and later on makes its periodical cleansing comparatively easy.

In the performance of the radical operation I believe that it always pays to attempt to close the Eustachian tube by careful curetting of its lining mucosa as far down as the isthmus. When successful, this must prove an important factor in attaining complete epithelialization of the cavity. Further, one should not forget that suppuration persisting from a radical mastoid cavity may be due to the presence of a fistulous tract from the petrous bone. Hence, during the operation careful inspection should be made to exclude such a possibility.

Where the amount of hearing present is useful to the patient, the radical mastoid operation is to be avoided whenever possible, particularly in children and young adults. The incomplete, or modified, or conservative radical mastoid operation was first described in this country by Heath in 1904. It aimed at conserving the function of hearing as much as possible, whilst eradicating the potential danger of a chronic suppurative disease. It consisted in opening up the attic and mastoid bony regions, removing diseased tissue but retaining healthy ossicles and as much of the tympanic membrane as remained.

Various modifications of this operation have been described by Cottle (1933), Lampert, Jenkins and others. However, the one that has found most favour with me is that described by Sourdille for another purpose, viz., the first step in his multiple operation on the mastoid prior to fenestration of the external semicircular canal in cases of chronic progressive deafness and otosclerosis. I have performed many operations of this kind, closely following his technique. It should be done only in very carefully selected cases, in which the hearing is good and the perforation is in the attic region or is small and marginal in the posterior segment of the tympanic membrane. The presence of cholesteatoma need not always prove a contra-indication to the operation. Regarding the ossicles I have come to the conclusion that unless covered by healthy mucous membrane, the incus and head of the malleus may as well be removed. If left, even though not necrosed, they later on become involved in the healing process. The fibrous tissue eventually binds them down and renders them immobile, thus from pressure effects making the final degree of hearing less than if they had been removed at operation. One admits that removal of the incus and head of the malleus (the latter to facilitate drainage only) invariably reduces the acuity of hearing. Nevertheless useful hearing is maintained. To my mind, the question of the conservation or not of the ossicles is of far less importance than the problem of how to maintain the mobility of the oval and round windows. If, as I believe, good hearing depends on the proper functioning of these windows, the one being in opposite phase and synchronous with the other, this, maybe, can only be achieved by an operation which leaves an air-space in the tympanic cavity, with the walls of the latter covered over by mucous membrane. Hence my contention that it is better to remove the incus at operation rather than, by retaining it, find it later on bound down by fibrous tissue and exerting a pressure effect upon the oval window via the stapes. This theory, too, can explain why, after the radical mastoid operation when the cavity remains moist, hearing is very often much better than in the completely epithelialized one. The continuity of the external auditory canal membrane with that of the tympanic membrane should be preserved, and drainage should be carried out via the post-auricular incision as in simple mastoidectomy. W. McKenzie (1940), published his results of 70 cases operated upon by the conservative radical method. My own results are about the same as his, viz. about 50% of dry ears with retention of good hearing. My technique, however, differs in that I have never yet made use of a meatal flap.

Since the field is so small and the technique both difficult and delicate, the surgeon is greatly facilitated in his work by the aid of binocular magnifying spectacles, good lighting and an efficient blood-suction apparatus. The same applies, of course, to other regions of mastoid surgery, but especially to that of the inner wall of the middle-ear cavity where magnification helps one to recognize important small relations and to carry out the necessary delicate instrumentation.

Otologists have often discussed the significance that lies in accidentally or purposely uncovering the dura mater and the lateral sinus in cases of otherwise uncomplicated

mastoiditis. I believe the answer is this: Never purposely lay bare these structures unless the bony disease leads down to them, but, when thus removed or accidentally so, bear in mind the fact that infection has been brought a stage nearer to the vital intracranial contents, and govern your subsequent proceedings accordingly. It is advisable to leave such a wound well exposed and very lightly covered with sterile gauze, rather than to close it up with possibly infected blood-clot. Penetrating wounds of the dura and sinus wall should be dealt with in a similar manner, though it may be necessary sometimes to occlude a grossly injured sinus above and below the site of injury and open up the intervening portion. Through neglect of these precautions one has seen not only rapid infection of the meninges but also fatal hæmorrhage from the subsequently infected lateral sinus.

Following the modern technique, skin and muscle grafts on the mastoid cavity should seldom be necessary after an uncomplicated simple or radical mastoidectomy. In plastic operations to close large post-auricular fistulæ, or to open up a stenosed external auditory meatus which is inadequately draining a suppuration from the middle ear, they may occasionally be used with advantage.

The respective merits of the post-auricular approach as compared with that of the endaural route, as advocated by Lempert (1928), has been well discussed by many aurists and the superiority of the latter method has not been substantiated. The fact that the majority of otologists still practise the old and original method is sufficient answer to the question. Indeed, a tolerant attitude becomes sceptical criticism when Lempert further advocates this approach for such operations as fenestration of the external semicircular canal for otosclerosis and those concerned with the various intracranial complications spreading from the middle ear and mastoid.

Injury to the facial nerve during the course of a radical mastoid operation is a distressing event both to the patient and to the surgeon. Although the utmost care may be exercised in clearing out the middle-ear cavity, a paralysis of the nerve may occur even though it be discovered only post-operatively. Especially one should be on the look-out for this in cases of cholesteatoma when dehiscences in the bony wall of the fallopian canal from erosion are so likely to occur. Fortunately, a fair proportion of these paralyses eventually recover, especially the post-operative ones. However, those that do not must remain an everlasting stigma or undergo attempts for their repair by one of the several methods of graft implantation or anastomosis with other cranial nerves. Even plastic surgery on the facial structures themselves, as practised by Gillies, may have to be tried. A full review of the methods employed for the surgical treatment of traumatic facial paralysis by direct nerve suture and graft inlay has been given by Miss D. J. Collier *et al.* (1941). Following the pioneer work of such men as Ballance, Ducloux and Young, future workers can and will obtain much better results.

The treatment of petrositis, associated or not with Gradenigo's syndrome, still presents a problem to the otologist. The diagnosis is undoubtedly helped by radiography, especially when the cranial nerves in relation to the apex of the petrous and to the posterior fossa show no clear evidence of irritation. The surgical treatment has been thoroughly reviewed by Ramadier, Watkyn-Thomas (1936), Kopetzsky (1933) and others, and each has advocated his own preferred method of approach to the cellular apex. It seems to me that one should adopt here as conservative methods as possible. Very often a simple cortical mastoidectomy suffices to clear up the symptoms of an acute petrositis, just as the radical operation following an acute exacerbation of a chronic middle-ear suppuration will do likewise. When, however, often after a latent period, the clinical signs and symptoms suggest an empyema of the petrous apex—usually readily confirmed by radiograph—further steps should be taken. The fistulous tract should be carefully sought for, and when found to be present in the region of the antrum or semicircular canals, its opening should be enlarged and the tract curetted right along its path until the pus is reached and can be evacuated. When the opening of the fistulous tract cannot be found, or it is in the region of the Eustachian tube opening, the route chosen should be behind the arch of the superior vertical canal in relation to the postero-superior surface of the pyramid. The approach via the tubal cellular tracts and carotid canal, as recommended and practised by Ramadier, is condemned by Kopetzsky as being far too difficult and hazardous.

Again, conservatism should be our attitude in surgical treatment of inflammatory disease affecting or invading the labyrinth. Our first duty should be to clear away the primary focus, whether this means simply incising a drum-head or performing a simple or radical mastoidectomy. Only if and when symptoms of meningeal irritation occur should we proceed further to the opening up of the labyrinth, preferably by the method of Neumann.

Perisinus abscess and extradural abscess are complications of mastoid disease which are admittedly difficult to diagnose before operation. As a rule they need not exercise our minds very much provided that at operation we do not disturb any granulations present, for these are Nature's barrier of defence against bacterial invasion. The wound should be kept well open and the patient carefully watched for further spread of infection to intracranial contents.

Before passing on to a consideration of the most serious of the endocranial complications of otitic origin, viz. meningitis, brain abscess and lateral sinus thrombosis, it may be useful here to mention the use of sulphonamide therapy and that of penicillin. Before the introduction of these powerful, selective, bacteriostatic drugs the prognosis in such cases was always considered grave. This led in turn to elaborate surgical methods of treatment which, in already enfeebled patients, and particularly in cases of acute diffuse suppurative meningitis, very often did nothing more than quicken or delay the fatal issue.

The sulphonamides, since their introduction about the year 1937, have already proved their worth and have decidedly altered our conceptions of how to deal surgically with these conditions. Likewise it seems probable that penicillin, after further trial, will do the same. Briefly stated, their value is as follows: These drugs will not by themselves, and unaided, cure infective disease produced by certain organisms, except perhaps in the earliest stage of invasion. When pus has begun to form in bone or soft tissues the inflammatory process may be retarded, with the so-called masking of symptoms, but not to the point where resolution can effect a healing of such abscesses. Cirillo (1942) has cited several cases which ended fatally owing to the too early use of this form of chemotherapy and the consequent masking of symptoms. Most of us have had similar experiences, and we have been taught that these drugs cannot replace surgical treatment if an undrained necrotic focus is present. The great increase (almost double) in the recovery rate since the introduction of chemotherapy has been clearly shown by Williams and others (1942) in their review of the literature on otitic meningitis and report of results five years before and since the introduction of chemotherapy. However, apart from this added use of the sulphonamides, their conclusions as to the best method of treatment do not materially differ from those arrived at in a discussion on the subject by Layton, N. Jory and Symonds (1934).

I lay great stress on the diagnostic value of lumbar puncture and examination of the cerebrospinal fluid in all cases of suspected endocranial infection. Increase in pressure above normal levels and an abnormal cytology of the fluid, in conjunction with ordinary clinical signs, nearly always give a positive indication that the vital structures of the endocranium are being attacked. If the focal area of infection has not already been removed by operation, this procedure should no longer be delayed. If, on the other hand, only after the initial operation has this evidence been gained, further operative measures, and certainly chemotherapy, must be introduced without delay. It must be remembered, too, that the proper concentration of these drugs is most important and can only be determined by a blood examination. Again, the prognostic value of lumbar punctures will keep us informed of the efficacy or not of our therapeutic measures.

Brain abscess, whether it be in the temporosphenoidal lobe or the cerebellum, is a matter of great concern both to the otologist as well as the neurosurgeon. I think that, as far as brain surgery is concerned, we otologists should recognize our limitations. Personally, from a review of my own cases of otitic brain abscess, I have found that I have been successful only when I have discovered the fistulous or necrotic tract leading to the brain tissue and, through this, with a minimal disturbance of adherent meninges, have been able to locate the pus and establish drainage into the abscess cavity. The neurosurgeon on the other hand has established for himself rules of procedure for dealing with the abscess, whether by decompression, aspiration or enucleation, or by a combination of some or all of these. Northfield (1942), in some recent publications, gives a full account of these procedures and shows how, influenced by the closed method of treatment of brain abscess by Clovis Vincent, neurosurgeons to-day are obtaining increasingly better results.

There is still considerable difference of opinion among otologists regarding the best method of treatment for lateral sinus infection. Controversial problems arise concerning the eradication of the septic clot in the sinus itself or its extension to the jugular bulb, or even beyond this to the internal jugular vein. There are conflicting opinions, too, about whether to resect the whole or a portion of the vein in the neck, to ligate it (i.e. sever it between ligatures), or whether to leave it severely alone. I will state briefly my views in the light of my own practical experience. The simple, modified or complete radical mastoidectomy should first be completed. The lateral sinus is then laid bare, particular attention being paid to the upper end by nibbling away the bony groove until healthy sinus wall has been reached. The vein at this upper end is then temporarily

plugged. The lower end is dealt with similarly, but if healthy vein has not been reached one stops short of the jugular bulb. A gauze plug is introduced here and the sinus is then opened and whatever blood clot it contains is turned out. As much of the outer wall is removed as possible. Tentatively, the upper plug is now released until one feels assured free bleeding has occurred, after which the plug is firmly replaced. The lower end is dealt with in a similar manner, but if no bleeding occurs the plug is dispensed with altogether. Bleeding sometimes occurs from the inferior petrosal sinus or the mastoid emissary vein, in which case light packing with gauze will suffice to control it. The wound is left well open and only lightly dressed with sterile gauze. I make a point of removing the plugs from the sinus at the earliest possible time, sometimes on the second or third day.

We come now to the question of the internal jugular vein. I confess I have never tied one in the past fifteen years, nor have I ever opened up the jugular bulb area. I was influenced towards this conduct by the fact that some twenty years ago I saw my chief, Mr. Norman Patterson, searching for the internal jugular vein in order to ligate it. Finding it thrombosed beyond the clavicle, he left it alone and the patient made a complete recovery. This led me to several conclusions which, rightly or wrongly, have guided my actions ever since. First, I believe that in a thrombosed sinus an aseptic clot always precedes the infected portion. Secondly, if one opens the sinus where the initial infection has occurred drainage is thereby established, the *vis a tergo* is removed and little if any further aseptic thrombosis takes place downwards towards the heart. Thirdly, the induration about the upper part of the internal jugular vein is mainly caused by the lymphatics draining the sinus and jugular bulb area, including that of the mastoid bony tip. This infection may often lead to abscess-formation deep in the muscular layers of the neck which will need to be opened by incisions in front of or behind the sternomastoid. Chemotherapy by the sulphonamides will play an important role nowadays in dealing with the toxæmia or blood infection. My record of cases in the past fifteen years of one hospital practice shows 19 recoveries out of a total of 23. I may have been merely lucky, or else, perhaps, there is something in what I say about it being unnecessary to tie the jugular. It is interesting to note that Singleton (1942) has recently recorded the recovery of six consecutive cases of this disease in which the vein was not ligated, and he too now questions the necessity of doing so. I believe that when rigors occur early in cases of lateral sinus thrombosis before operation is undertaken, they do so whilst the thrombus is forming, when toxins, infective emboli or even isolated organisms may be entering the blood-stream. After thrombosis is complete toxæmia may still produce rigors, but emboli and organisms are excluded from the blood-stream. Metastatic abscesses in the lungs, joints and other regions of the body may occur after operation, but I think they are the expression of the earlier septic emboli which have got through the vein before complete thrombosis has occurred. Hence to prevent these, it would be too late to tie the jugular if at operation we have cleared out the infected clot completely or have left behind a thrombosed vein in the lower portion.

Suitable operations on the mastoid for the relief of tinnitus, vertigo and deafness have exercised the minds of otologists ever since mastoid surgery began. However, in the last twenty years or so, along with our advance in the theories of equilibrium and hearing, these have been mainly directed towards operations on some part of the labyrinthine capsule. In Ménière's syndrome complex when the membranous labyrinth itself is considered to be at fault and other factors have been excluded, a variety of operations have been advocated and practised. Since we do not yet fully understand the aetiology or pathology of the condition, although Hallpike and Cairns (1938) have so far given the best explanation, we cannot hope to be completely successful in our operative procedures. Portmann's operation on the saccus endolymphaticus, Dandy (1941) and other neurosurgeons' section of the 8th nerve, Wright's injection of alcohol into the exposed tympanic membrane and the oval window, Mollison's injection of alcohol into the external semicircular canal and Cawthorne's modification of this without alcohol injection, have all given fairly good results. My own feeling in the matter is that medical treatment on the lines recommended by Tobey (1941), Dederding, Mygind, Furstenberg and others must continue to suffice for the majority of sufferers, but if and when an operation must be performed, Wright's method should first be tried, but if unsuccessful, fistulization of the external semicircular canal via the mastoid approach should be recommended. For the alleviation of deafness of the chronic progressive conduction type much experimental work on the labyrinthine capsule has been done by Holmgren, Sourdille, Lempert and others. This has been well reviewed by Kopetzsky (1941), who presents the difficulties, apart from the delicate surgery involved, in obtaining lasting beneficial results. The external semicircular canal seems to be the site of election for the fenestration. No method, however, has yet been devised for ensuring the patency of this artificial

window, or rather its mobility. Sooner or later it becomes fixed, either by fibrous tissue or by the osteogenesis that takes place there. This, in my opinion, is the same problem that confronts us in the case of the modified radical mastoid operation, viz. how to ensure the mobility and hence the reciprocal action of two membranous windows, whether they are those provided by Nature or artificially provided by us. Until this problem can be solved it seems to me that we will not progress much further in helping to alleviate this type of deafness. In the meantime increasing help can doubtless be expected from the rapidly improving electrical aids for hearing by bone conduction.

In conclusion I shall merely mention some rare diseases that demand mastoid surgery. A gumma of the mastoid I have never seen, and tuberculosis only on a few occasions, in one of which, however, the whole of the petrous bone showed itself at operation to be a complete sequestrum. A dead labyrinth and a facial nerve paralysis were attendant factors. Again, I have seen during the past six years two cases, confirmed by operation, of a rare pathological condition, viz. hæmangioma of the petrous bone invading the middle-ear cavity and the posterior fossa of the skull. In the one case I was associated with Mr. Mollison and with him performed a modified radical operation. The case was then taken over by Mr. Northfield, who attempted the removal of the growth from the posterior fossa and petrous bone. A course of deep X-ray therapy followed operation with apparently satisfactory results. The other similar case was dealt with in conjunction with my surgical colleague, Mr. Broster, but has since been lost sight of. With regard to cases of cavernous sinus thrombosis I have only seen one in the whole of my career, and that ended fatally.

The occasional malignant disease of the ear and mastoid can still only be dealt with palliatively by a combination of surgery, diathermy and X-rays.

In conclusion may I add that I hope I have raised in this Address some useful points for discussion, from which, too, there will arise a consensus of opinion that will serve to help us when dealing with future problems of mastoid surgery.

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Mr. W. M. Mollison: Choice of operation in chronic suppurative otitis. In young people I feel that the radical should not be done on account of the loss of hearing after it and in view of the powers of recovery of function in the young. Unless the malleus and incus are found necrosed some form of conservative operation should be followed, only proceeding to the radical if conditions finally necessitate it. One of the essentials for success is a generous meatus and the President has stressed this by his treatment of the deep free end of the soft tissues; in many cases a temporal muscle flap is helpful. Incidentally this temporal flap is the only method of closing post-aural fistulæ with 100% success.

These two tables show the hearing after various operations; they are the result of the examination of recruits referred from medical boards and show the results of the operations. Hearing is good if the man heard 10 ft. and upwards, bad if he heard 0 to 6 in. and fair in between.

TABLE I.—186 MEN, AGED 17-25.

Radical operation	10 (dry 4)
Hearing bad	9
Hearing fair	1 (facial paralysis 1)
Conservative operation	17 (dry 6)
Hearing good	4
Hearing fair	7
Hearing bad	6
Heath's operation	1
Hearing poor	1
Simple operation	14
Hearing good	9
Hearing fair	4
Hearing bad	1

42 = 22.5%.

TABLE II.—205 MEN, AGED 25-42.

Radical operation	9 (dry 5)
Hearing bad	8 (1 not known)
Conservative operation	7 (dry 0)
Hearing bad	7
Simple operation	8 (dry 4)
Hearing good	24 operations (dry 9)
Hearing bad	9
Hearing fair	4
Permeatal operation	1
Hearing bad	1
					25 = 12.2°.

A recital of possible mishaps during operation on the mastoid may be encouraging as showing what Nature can do in the way of recovery.

(a) Opening the mastoid under the impression that there is a posterior marginal perforation with granulations and pus, only to find the mastoid normal and the granulations due to local necrosis of the tympanic ring—always annoying.

(b) Letting the gouge slip in the wrong place; on one occasion my gouge slipped and punctured the dura above the tegmen antri, while operating on an acute mastoiditis. The operation was completed. The temperature and pulse charts were watched; in three or four days the temperature became subnormal and the pulse slowed and the patient vomited. The wound was then opened and a subdural abscess evacuated and uninterrupted recovery followed.

(c) Puncture of the lateral sinus during operation for acute mastoiditis; a child developed signs and symptoms of thrombosis in a few days; the internal jugular was ligatured and the patient recovered.

(d) Damage to the facial nerve; an elementary knowledge of the anatomy of the position of the nerve should save it from damage and indeed it is rare to see a paralysis in these days. However, I have damaged it on three occasions (this is as far as my memory takes me) and in all three it was in cases of very brittle and hard bone; (1) In operating for acute mastoiditis, opening the cells running down immediately posterior to the nerve in its canal, the bone cracked across the canal and facial paralysis resulted and I fear was permanent. (2) During a radical operation—the same accident, but in this case recovery occurred in a few weeks. (3) In an operation to open the external canal, the bone was seen to crack—it was pressed back into position—the operation of opening the canal was completed. The resulting paralysis had completely disappeared in three weeks.

Mr. F. W. Watkyn-Thomas said that Mr. Mollison's rubber-dam technique was most valuable; it made dressings as nearly painless as mastoid dressing could be.

The epitympano-mastoid operation without plastic flap was introduced by Bárány about twenty years ago, and was widely used for some time in the Northern European clinics. He had done a number himself, but he had found that, in spite of some excellent results, too often a secondary plastic was needed to provide drainage. This was a general experience; Jessen of Copenhagen found that in 71 cases of this operation there was complete healing in only 58% of cases, and in eight years S. H. Mygind found that of 31 cases of mastoids requiring further operation 22 had been treated by this method. He felt that the President's excellent results were due to the skill of the operator, not to the propriety of the operation. He agreed that preservation of the ossicular chain was not the most important factor in the preservation of hearing. The important thing was to leave enough of the drum to protect the inner wall. So far as hearing was concerned it did not matter materially whether the incus was removed or not. If an incus was so loose that it would come out at a touch of the hook it was clear that the continuity of the ossicular chain was broken already, and the incus should be removed as a useless foreign body.

In the last 12 cases of lateral sinus thrombosis which he had seen 8 bled freely from both ends when the sinus was opened, and no interference with the jugular was needed. In one, the only fatal case, there was no bleeding from the upper end; the patient died of a cerebral thrombophlebitis. In 3 there was no bleeding from the lower end. One patient recovered without further trouble. In 2 swinging temperatures continued and the vein was tied. Both patients recovered. Perhaps they would have recovered anyhow, but they did not look as if they would.

When he ligated the jugular he always preferred to divide it, bring the upper end to the surface, and tie all branches above the point of section.

Mr. T. B. Layton said that during the last twenty-five years otologists had learnt to be conservative when treating mastoid cases.

He did not believe to-day that the simple incision for the post-aural swelling should ever be done until pus had formed which could be felt by fluctuation. It was surprising when this plan was adhered to how many recovered without any operation at all. The only exceptions to this rule should be when rigidity of the neck, indicating meningeal irritation, was present, or where a rigor had occurred, suggesting sinus invasion; and both these were very rare in cases with a retro-aural swelling. A snick should be made and a tube put in for forty-eight hours. He now believed that no mastoid operation should be performed on a patient with a retro-aural swelling until pus had formed and that snick had been made.

They had also learnt that chronic ear disease was an incurable condition. Ear disease had to be tackled from an earlier stage than at present. In the population it was to-day dealt with from the schools. That was too late. It had to be dealt with before the child got back to the school after the acute ear disease had occurred.

Mr. E. Cowper Tamplin said that for three years now, with the aid of sulphathiazole insufflated at operation, he was discharging about 80% of cases of acute mastoid in eight days, soundly healed with a dry middle ear. It was doubtful if this could be further reduced with penicillin.

Mr. I. Simson Hall said that in chemotherapy a weapon had been found so effective against the serious complications of otitis media that the possibility of a fatal termination was slender, and all our skill could now be directed towards the preservation of function in the ear affected.

Those whose duty it had been to examine recruits for the Forces had been impressed by the wastage of otherwise high-grade man-power owing to the results of otitis media.

The large number of low-category men and women was convincing proof that it was time the treatment of otitis media was replanned with restoration of function as the criterion of success.

Mr. Terence Cawthorne made a plea for abandoning the term "conservative-radical" operation in favour of "modified", adding if necessary a descriptive but not contradictory adjective.

For the past six years he had used the endaural approach for the uncomplicated radical operation where the mastoid was acellular. He had found that with practice this approach offered certain advantages over the formal operation.

To avoid exposure of the dura of the middle fossa, he recalled Arthur Cheatle's advice on the subject of what to do when in doubt as to the whereabouts of the mastoid antrum: "Remove the tegmen and follow the dura inwards. You will always find the antrum without jeopardizing the labyrinth or facial nerve". His experience of facial nerve surgery had been that often the nerve had been damaged in the course of a mastoid operation because the operator had tried to search for the antrum too far down. Whilst it was clearly not necessary to expose the dura in every case, its value as a landmark and guide should be remembered and taught.

Bleeding from a lateral sinus accidentally injured could usually be checked by the application of a small square of temporal muscle. The advantage of this over plugging was that the lumen of the sinus was not encroached upon.

The work of Hallpike and Cairns, Wright, Crowe, Rollin and Fowler had established a pathological basis of sufficient stability to warrant the use of the term "Ménière's disease" in many cases of vertigo and deafness, and he hoped that the terms "symptom complex" and "syndrome" as applied to Ménière might be abandoned.

Brigadier Myles L. Formby said that it was the skill with which the atticotomy was performed and the subsequent meticulous care with which the President always personally treated his cases that were the important factors. It was useless to do the operation and leave the after-care to somebody else; suppuration invariably continued and although the ear might no longer be dangerous the result would certainly not be satisfactory.

Concerning the drainage of brain abscesses he agreed that where the track was obvious, the dura necrotic and the abscess at or near the brain surface in relation to the mastoid wound, it should be opened and drained. For all other cases the correct procedure was repeated aspiration through healthy dura. If the dura exposed in the wound were thoroughly cleansed then exploring the temporo-sphenoidal lobe was not a dangerous procedure. Success in the treatment of brain abscess depended on resistance to the spread of infection by the surrounding brain tissue and removal of the pus. The latter could not be achieved by drainage, at any rate not for any length of time, except in a few abscesses that were very near the surface.

Mr. R. D. Owen said he would like to know whether the President still regarded mastoid drainage, in childhood, as the right or the wrong thing to do where the case presented normal temperature and no mastoid tenderness but a pulsating discharge persisting for five or six weeks after the initial onset.

Although one might rely on sulphonamides for resolution and an intact drum, one must not forget that these cases of subacute mastoiditis if left without drainage could lead to permanent deafness. It was quite likely that a good number present themselves in middle age with progressive deafness associated with Ménière's disease. He felt that a timely paracentesis or mastoid drainage would avoid this disability in adult life.

The President (in reply) said that he dispensed with the meatal flap as far as possible, for he looked upon the external auditory meatus as a by no means unimportant structure for the hearing function.

For drainage after a simple mastoidectomy he used a fine rubber tube containing a wick of narrow ribbon gauze which was left in place for forty-eight hours in order to form a channel down to the antrum for further drainage with a gauze wick only. From many years' experience he found alcohol (50%) an excellent bactericide and since using it as a routine had seldom been troubled by secondary infection of the wound. He certainly agreed that there was an increasing tendency to close the wound at the time of operation.

Preservation of hearing was a very important factor in mastoid surgery, and in this respect the conservative mastoid operation had proved its value. The removal of the incus meant usually no more than a loss of acuity in hearing. If there was more than this loss of acuity one must look elsewhere for the impairment, for example, in the round or oval window or in the nerve itself.

Exposure of the dura should always be considered as a potential danger of infection to the intracranial contents and treated accordingly.

[December 1, 1944]

DISCUSSION: TREATMENT OF ENDOCRANIAL COMPLICATIONS
OF OTITIC ORIGIN

E. D. D. Davis: *A brief review of the treatment of abscess of the temporosphenoidal lobe of the brain arising from the ear.*—By reviewing the treatment of a temporosphenoidal abscess I hope to demonstrate that this abscess should be approached and drained from the mastoid area. If drainage fails to achieve a satisfactory result in a very few chronic encapsulated abscesses then enucleation may become necessary.

The drawings of three specimens are shown to illustrate the pathology of a brain abscess. The first two are frontal lobe abscesses because they are the best specimens I could find in the London Pathological Museums.

The first drawing (fig. 1) is a large abscess due to a sharp slate pencil which had penetrated the roof of the anterior cells in the lateral mass of the ethmoid. The point of the



FIG. 1.—Large abscess in the left frontal lobe of the brain, arising from a foreign body in the nose (Charing Cross Hospital Museum), see also colour plate *Proc. R. Soc. Med.*, 1934, 27, facing p. 1,288.

pencil projected into the anterior fossa of the skull for 2 cm. The patient was a boy of 17 who was comatose when admitted to hospital and in consequence it was not known when the slate pencil was pushed into the nose. The boy fell on the pavement on the way home from school, he was unconscious for a few minutes and his neurological symptoms commenced from that day five years before he was admitted to hospital comatose; hence it is probable that the abscess is of about five years' duration. The dura mater and arachnoid in relation to the slate pencil were thickened, opaque and adherent to the brain but there was no subdural or extradural abscess. The abscess cavity measures 4.5 by 5 cm. It is irregular in shape and partly enclosed by a fibrous wall or so-called capsule surrounded by oedematous brain substance. Toward the outer side a recent extension of the pathological process has occurred where a considerable amount of brain substance is seen in various stages of necrosis. In this position a locus is forming and it is found frequently that a temporosphenoidal abscess extends in this way in its deepest aspect towards the descending horn of the lateral ventricle. The formation of a capsule appears to depend on the resistance of the patient and on the virulence of the infecting bacteria. The abscess is more likely to be walled off when the infection is caused by the *Bacillus proteus*, *Bacillus coli* or staphylococci than by the virulent streptococcus or pneumococcus. An encapsulated abscess is more common in the frontal lobe than in the temporosphenoidal. More frequently a foreign body such as a fragment of bone or a missile lodged in the brain is walled off and may cause an abscess some time later. The pulsation of the brain tends to extrude the encapsulated abscess particularly if the capsule is uncovered by removing a cap of the adjacent brain tissue from its surface. A few but not all chronic abscesses may become encapsulated and it is stated that the capsule may be firm enough to permit enucleation in from eight to twelve weeks. During this period the patient may

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Preservation of hearing was a very important factor in mastoid surgery, and in this respect the conservative mastoid operation had proved its value. The removal of the incus meant usually no more than a loss of acuity in hearing. If there was more than this loss of acuity one must look elsewhere for the impairment, for example, in the round or oval window or in the nerve itself.

Exposure of the dura should always be considered as a potential danger of infection to the intracranial contents and treated accordingly.

a dura mater hook in the area where the dura is thickened, covered by granulation tissue or by an extradural abscess. If the dura is normal in appearance the incision is made in the area covered by the roof of the mastoid antrum. If an abscess is present, in my experience pus escapes with the first thrust of a large needle or sinus forceps. Care should be taken not to lose the abscess and the needle is left in situ until the largest size aural speculum or an encephaloscope is slipped over the needle into the abscess cavity. Pus and debris are removed by gentle suction. If irrigation is employed it must be gentle and Ringer's solution or blood plasma should be used through the speculum. Weed and Wegeforth (1919) of the Rockefeller Institute injected the subarachnoid space of cats with antiseptics and found that chloramine, flavine and mercurochrome caused intense reaction and convulsions. Isotonic saline alone caused toxic and convulsive effects but Ringer's solution is tolerated well. Two small rubber drainage tubes stitched together are inserted into the abscess cavity through the encephaloscope. The tubes must be firmly anchored by stitches and by a reinforced firm dressing of rolls of gauze built up round the tubes to hold them in position. Various types of tubes and methods of drainage have been advocated. Packing the abscess cavity with gauze does more harm than good and should be avoided. Lemaitre's method of introducing the smallest drainage tube followed at frequent intervals by larger and larger tubes is unsatisfactory. If drainage tubes could be avoided results might be better. The dressing is untouched for six days and at this, the first dressing, preferably done in the operating theatre, the drainage tubes are removed and if there is no escape of pus the wound is allowed to close even at the risk of having to open the abscess again.

The advantages of approaching the abscess from the mastoid area as described are: (1) The source of infection can be eliminated. Extradural abscess and lateral sinus thrombosis, when present, are dealt with. Moreover the condition of the dura found at this operation will either confirm or correct the diagnosis. In some cases the important early diagnosis cannot be made without exploration. (2) The track of infection is followed where the spread of infection in the subarachnoid space is prevented by adhesions. Two cases seen by me in which an osteoplastic flap was made in the temporal region died of meningitis. (3) The lowest point of the abscess, and where it is nearest to the surface is drained. (4) The area of operation can be sterilized as well as any other part of the skull.

Treatment by aspiration without any form of drainage between the tappings has been condemned by Cairns (1934). The abscess cavity fills remarkably quickly, especially when there is any oedema of the brain. Aspiration of an abscess in other parts of the body is not a satisfactory procedure.

Enucleation of the abscess is possible only when the abscess is completely walled off by fibrous tissue. In a few cases encapsulation takes eight to twelve weeks during which time the catastrophic of meningitis, rupture into the ventricle or oedema of the brain may occur. Loculation and particularly multiple abscesses make enucleation difficult. When the neurosurgeon found enucleation difficult and unsafe he has resorted to marsupialization. There is no evidence to show that epilepsy is more common in abscess which has been drained than that subjected to enucleation. If neurological signs and symptoms persist after drainage or if there is a permanent sinus then enucleation is probably desirable.

Marsupialization is done on rare occasions as an expedient when enucleation is unsafe or impracticable. It has always been an unsatisfactory operation for cysts in other parts of the body when they could not be dissected out.

The results of various methods of operation are difficult to express in figures. The large majority of brain abscesses are not seen until the patient is drowsy, comatose or in the terminal stage and are complicated.

The *Proceedings of the Otolological Section* records a large number of successful cases treated by drainage only. At one meeting in 1927 18 successful cases were recorded and whenever the subject of brain abscess has been discussed a number of successful cases are shown.

Results of operation.—Macewen, 80% survived. Neumann, 47% uncomplicated cases survived; no organisms in C.S.F. Fraser, J. S. (1930), 17; 6 cases survived, 33% approx.; 6 meningitis before operation. Davis, 28; 4 uncomplicated cases survived. 24 post-mortem complicated cases.—11 meningitis before operation; 7 ruptured into the ventricle; 4 oedema of the brain; 2 multiple abscesses.

Northfield's (1942) analysis of 24 cases of brain abscess: 9 cases drained, 2 survived—cause of death not stated; 15 cases not drained, 10 survived=8 enucleated, 2 aspirated. The 7 drained cases which were fatal may have had meningitis or some terminal complication before being drained. It is assumed that the 8 successful cases of enucleation were encapsulated and therefore were more favourable than acute cases.

succumb to meningitis, rupture of the abscess into the ventricle or from œdema and encephalitis, the usual termination of a fatal brain abscess. Moreover multiple abscesses, deep loculi and recent extensions make enucleation impractical and not without risk. The specimen shows a marked enlargement of the left cerebral hemisphere as a result of œdema. The anterior horn of the lateral ventricle is obliterated and the basal nuclei are distorted by compression. This patient died of œdema of the brain and encephalitis with Cheyne-Stokes' breathing. The second specimen, not illustrated, shows multiple abscesses arising from chronic suppuration of the frontal sinus and the damage done by a drainage tube introduced into the brain (see colour plate, *Proc. R. Soc. Med.*, 1934, 27, 1286). It emphasizes the necessity of placing the drainage tube accurately into the cavity of the abscess and of anchoring the tube by two stitches to the deep fascia reinforced by a firm and suitable dressing. As a house surgeon I assisted my chief, a general surgeon who at one time was assistant to Macewen, at this operation and there is no doubt that the large drainage tube was introduced into the cavity of the abscess and anchored by a stitch. It is presumed that the pulsation of the brain displaced the tube. The pulsation of the frontal lobe is always more marked than that of the temporo-sphenoidal. This patient died of cortical meningitis which was present before the drainage operation was performed.

Fig. 2 indicates the commonest site of a temporo-sphenoidal abscess of otitic origin. It is immediately above and behind the roof of the mastoid antrum with a stalk approaching the surface. It is probable that this abscess would have been missed by an exploratory burr hole or even by an osteoplastic flap which is usually made in the temporal fossa above and in front of the ear.

Fig. 3 illustrates the approach to a temporo-sphenoidal abscess through the mastoid process.



FIG. 2.—Brain in section, showing space left by encysted abscess in temporo-sphenoidal lobe. (Copied from William Macewen, "Pyogenic Infective Diseases of the Brain and Spinal Cord," 1893, p. 94, Glasgow.)

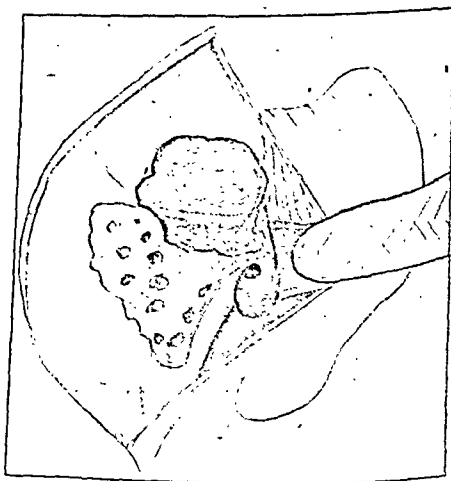


FIG. 3.—Second stage of the operation in which the two openings in the skull are converted into one. (After Hunter Tod, *Burghard's System of Operative Surgery*, 1914, p. 309, London.)

The mastoid operation is done without the mallet by using a skull gouge with the hand and a nibbling forceps. When a diagnosis of an abscess has been made or suspected, the dura is thoroughly exposed by removing the roof of the mastoid antrum and tympanum, then a burr hole is made in the squama of the temporal bone. The bony aperture is enlarged in all directions by nibbling forceps and there is no limitation to the extent of the area of dura exposed. The wound and the area are thoroughly cleansed by ether and a 1:1,000 flavine solution. Clean towels, clean gloves and instruments are now used before the dura is opened. The mastoid wound can be cleansed just as efficiently as the skin of the scalp over the temporal area where the neurosurgeon approaches the abscess away from the ear. This point is proved by the fact that the temporo-sphenoidal lobe has been explored on many occasions without any sepsis or harmful results. The exposed dura is isolated and its blood-vessels compressed by packing sterile gauze between the bone and the underlying dura. It is desirable to follow the track of infection from the mastoid to the brain. Therefore a small crucial incision is made in the dura using

condition at all; I think it is a blood invasion and should be treated as such. Here the aural tract is the victim, not the focus, and opening and draining it will be quite useless. For drainage of the labyrinth I have nearly always done the "double vestibulotomy" which is safe or simple. I have done the Neumann operation, but I do not find it either safe or simple. In the actual technique of the operation I think it is most important to have really sharp chisels and gouges. I have not yet had the good fortune to use an operating microscope, but I have found v. Eicken's magnifying loupe useful, but cumbersome. The danger to the facial nerve is—it seems to me—usually at the postero-inferior corner when one is working on the recess of the round window. Injury to the columella should be avoided, as the area is flooded with cerebrospinal fluid. I have seen this happen once or twice, but it has never done the least harm to the patient—all the same it is an accident to be avoided.

In latent labyrinthitis the operative findings dictate the procedure on the labyrinth. If the whole wall is covered by scar tissue, leave it alone; if there is a fistula into the dead labyrinth, enlarge it for drainage; if the labyrinth has sequestered, take it out. In the last two years I have not used transabyrinthine drainage for meningitis of labyrinthine origin, because I think that the continual escape of cerebrospinal fluid makes it more difficult to maintain the requisite high concentration of sulphonamide. That does not alter my opinion that, in its day, it was the greatest advance in the surgery of the condition.

By petrous invasion I mean any extension of disease into the body of the petrous; I most emphatically do not limit it to invasion of the apex, which I think is uncommon. About 35% of adult petrous bones are fully pneumatized, and in most of them some marrow persists. But, whether pneumatized or not there is a hard shell to the bone, with an excellent blood supply, and sequestration or perforation into the cranial cavity is rare. Also, the more complete the pneumatization the more complete the obliteration of the vessels passing from dura to bone and the less the risk of spread by these tracks; on the other hand, in the non-pneumatized bone the marrow is capable of stout resistance. For these reasons a petrous infection can usually be treated with deliberation.

A considerable majority of petrous invasions clear up entirely with an adequate mastoid operation and careful follow-up of any deep cell tracts—especially the group of cells in the petrous angle. I have seldom seen the sublabrynthine cells. I think the rarity of the condition is a testimony to the care with which we do our acute mastoids. Of course there are cases in which the dangerous cells are so shut off by bone that they are absolutely undetectable at a first operation; these are the cases where petrositis develops some days or weeks after a mastoidectomy. In such cases the onset is seldom dramatic, an increase of discharge, a recurrence of pyrexia, sometimes—by no means always—retro-orbital pain, are the usual signs. Odd little disturbances of the labyrinth are not uncommon. Occasionally there is just the suspicion of a facial weakness. I do not think that in these cases operation is indicated immediately; it may not be indicated at all. Radiographs of the petrous pyramids should be taken; the optic discs should be watched most carefully; at the slightest suspicion a lumbar puncture should be done—and on no account whatever should we yield to temptation and mask the signs by sulphonamides. If there is any evidence of meningeal irritation, operation must be done forthwith; otherwise, unless pain and headache increase, or the pyrexia continues I am inclined to wait. The longer one can wait the more likely one is to find a track of carious bone and infected cells to follow. I do not think that a 6th nerve palsy is necessarily a proof of apical invasion, but whenever I have seen this sign in a case of petrositis I have always found other indications, such as increasing pain, for operation. As to the method of operation I have always said that we are not engaged on the anatomical exercise of finding the apex, we are doing the surgical routine of hunting the pus, and our object is to protect the meninges. For this reason I have never done the Almour-Kopersky operation. Although this is a most ingenious route to drain an abscess of the apex, it would not afford adequate drainage for the even more dangerous extradural abscess. The Ramadier operation has the same disadvantage, and as well seems to me unnecessarily dangerous. I have either followed up any available track, or where I could find none, have done the Voss-Ruttin-Eagleton method of unlocking the petrous. I have had no personal experience of approach by the endaural method, nor have I ever succeeded in finding a track through the arch of the superior canal, which Paul Frenckner has described. On three occasions I have seen a forward extension, probably through the zygomatic cells. On a previous occasion I have mentioned invasion of the superior petrosal sinus and spread to the lateral, but I have not seen such a case since these were reported. I have never myself seen an extension into the pharynx, but there certainly are such things. The possibility of approach to the petrous by a nasopharyngeal route has been suggested by Russell Burke, but as far as I know it has only been worked out on the cadaver.

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F. W. Watkyn-Thomas: *Labyrinth and petrous infections.*—Although these are not intracranial infections themselves they are so frequently a cause of such infections that it is fitting to consider them here. Under modern surgical conditions neither of these complications is often seen.

For practical purposes the problem of the infected labyrinth is a problem of meningitis. It is remarkable how seldom labyrinthine infections cause cerebellar abscess. This statement is upheld by the figures of Zange and the statistics of the Edinburgh Royal Infirmary. Lateral sinus thrombosis as a result of labyrinth infection occurs as a curiosity. (I have only seen two.)

Extension from the labyrinth may be through the internal auditory meatus (usually), through the bone (sometimes), along or through the aqueduct of the endolymph (rarely), and through the aqueduct of the perilymph (perhaps). The treatment of labyrinthine suppuration is entirely conditioned by our view as how best to avoid such intracranial invasion.

If the labyrinth is alive, it is most unlikely that it is infected. If therefore we find a fistula—or, more accurately, an erosion of the labyrinth wall—with an active labyrinth, especially if the so-called fistula sign is present, that labyrinth should be left severely alone. The proper treatment is the adequate mastoid operation and rigid non-intervention as far as the labyrinth is concerned.

If the labyrinth is so very dead that it is a sequestrum, of course it has to come out.

Last, if the labyrinth is dead and the patient already has meningitis the general opinion is that the labyrinth is a probable—or at any rate a possible—focus, and should be drained accordingly. I am not referring here to translabyrinthine drainage of the cisterna pontis; that is quite a different problem.

The principal difference of opinion is what to do when the labyrinth has been killed in the course of a suppuration and the patient has not yet got meningitis. Two conditions are recognized: (1) In the course of a middle-ear suppuration the labyrinth is destroyed by infection, with all the characteristics of a "labyrinth storm". (2) The patient has a suppurating ear, totally deaf, and dead to caloric tests. Sometimes he can remember severe vertigo, perhaps diagnosed as "gastric influenza", somewhere in the remote past. Sometimes he cannot even remember that. The first condition is "manifest labyrinthitis"; the second "latent". In manifest labyrinthitis without meningitis we may safely assume that, as the labyrinth has been destroyed by an aural infection it is itself infected, and so is a danger to the meninges. According to one view, once the labyrinth has been so killed it is a potential danger and should be drained forthwith. Granted that we cannot be certain that it is a suppurative rather than a serous labyrinthitis, it is unusual for a serous labyrinthitis to show complete loss of caloric response and total deafness; if it should, it is highly unlikely that any useful hearing will survive. The other view is that by early operation we may precipitate the very disaster which we wish to avoid, as well as destroy a labyrinth still capable of recovery. Therefore, do not drain the labyrinth until there is definite evidence of meningeal irritation, e.g. a rise, however slight, in the cerebrospinal fluid cell count.

My personal experience, from 1920 to about 1940, was that of all cases of suppurative labyrinthitis which came into my hands, *before any meningeal signs could be detected*, I lost only three—one, an anesthetic fatality due to unsuspected myocardial degeneration, one by a spreading necrosis of neighbouring bone (the only case of the kind I have ever seen) and one where I persuaded myself that it would be safer to wait a few days. I was wrong, that patient died of meningitis—I do not say it was cause and effect, I hope it was not, but that was only one in the series. Now, with sulphonamides available, if meningitis should appear there is a good weapon at hand to deal with it, because the bony labyrinth is the only bony cavity in the body where sulphonamides do not act at a great disadvantage. We know that they freely enter the cerebrospinal fluid, and we know that the perilymph is in continuity with that fluid, therefore we can reasonably hope to destroy the organisms in the labyrinth by chemotherapy. At present I feel that the right procedure when labyrinthitis appears in the course of a chronic, a recurrent, or a sub-acute suppuration, *provided always that there are no signs of meningeal irritation as proved by lumbar puncture*, is to load the patient with sulphonamides and, when all is quiet, to do the radical operation and to complete it by opening the labyrinth, just as one opens up any other cell system in an infected area. You may have noticed that I have excluded acute suppuration. I do not believe that the acute fulminant condition in which middle ear, labyrinth and meninges are invaded almost simultaneously is primarily an ear

features about which information is sought when the cerebrospinal fluid is first examined. At that time or later additional information may be desired such as chlorides, sugar, protein and sulphonamide content.

Certain types of meningitis, especially if they occur following long-standing suppurative otitis media, where the labyrinth has been invaded, show a fairly high proportion of lymphocytes in the fluid, and it may well be that the number of lymphocytes furnishes some idea of how long the infective process has been going on.

Treatment.—Before anything else is done the patient with meningitis requires chemotherapy. But there are certain cases which require surgery in addition, namely, the third group of which I have spoken, in which there is bone destruction. I think that only an otologist can decide which cases require surgery and to overlook such cases is to invite a relapse, possibly fatal. It is not always easy, when a patient has a discharging ear and meningitis, to decide whether or not there should be an operation. An otologist is in the best position to decide this, particularly if he can think in terms of the type of infection and the way it has spread. In fulminating cases the spread to the sub-arachnoid space is rather like the spread of fog into a house, underneath the door and through any crevice, and to undertake extensive mastoid surgery will not hinder the spread but will jeopardize the patient's chance of survival. The same applies to the cases of vascular spread and I feel that early mastoid surgery should not be embarked upon in any case of meningitis following within a few hours or days of an otitis media.

But in the third type of case, where there is disease of some weeks' standing, mastoid surgery with removal of diseased bone is required, and the only question there is *when*. These cases are on the whole better left for a day or two—it is difficult to lay down any hard and fast rule. I now think that it is best to start a course of one of the sulphonamides before operating. My experience with sulphadiazine is small, but from what I have read I am led to believe that it is probably the best of the sulphonamides to use. Nor have I any personal experience of penicillin in meningitis. The one drawback to penicillin is that it has to be given intracisternally or intrathecally.

As to the introduction of various sera into the thecal space I have always felt very strongly that the less one introduces into the theca or cisterna the better, for with but few exceptions—and I believe penicillin is one—intrathecal medication does more harm by irritation than good by combating infection.

Mr. F. McGuckin: My interest in brain abscess was aroused in dramatic fashion some fifteen years ago, when I watched a lateral ventricle rupture through a temporal lobe abscess, the peripheral wall of which had just been incised. This was the first of three such cases published in the *Lancet* in 1936. All three recovered. By 1935, 100 cases of abscess had been summarized, 39 of which were personally surveyed in part or in whole. Though interest remained, enthusiasm was curbed, first by the ups and downs of good and bad runs of cases, and secondly by the unfortunate sequelæ, fits for example, in some of the recovering temporal cases.

In the series, the causes of death fell roughly into two groups: those from diffuse cerebrospinal infection usually by ventricular erosion, and those resulting from pure pressure exerted finally on the medulla. Correct timing of intervention, if this were possible, was clearly the preventive treatment of the first accident. The pressure factor suggested the cardinal importance not merely of timing but of so limiting intervention as to avoid increase in tension from traumatic oedema.

The study of the morbid anatomy of brain abscess is important. The part played by the Virchow-Robin space in the transmission of temporal abscess is clear enough; though I think not enough attention has been given to the superior petrosal sinus or to thrombosis of veins included in a localized patch of leptomeningitis.

Up to 1935 I had not personally surveyed a single case of cerebellar abscess, alive or dead, in which a labyrinthine transmission was proved to my satisfaction, and in the 100 cases already mentioned there were but 2 out of 44 cerebellar abscesses in which a labyrinthine origin was clearly demonstrated, one via the posterior semicircular canal and one via a saccus empyema. In my experience lateral sinus thrombosis has accounted for nearly half the cases, and it was responsible for both my cases of non-suppurative cerebellitis. The mechanism is that of retrograde thrombosis of communicating veins. On the score of the mechanics of internal hydrocephalus, which may be extreme in temporal lesions, tribute must be paid to the brilliant work of Jefferson and Rowbotham on tentorial pressure cone due to herniation of the uncinate process of the temporal lobe. This work, for me, ended ten years of confusion about the matter.

I believe there are three features which suggest that the otologist may justly retain some place in the conduct of this disease. First, the mastoid approach sometimes locates an abscess with very great accuracy and often with much greater accuracy than the neurosurgical approach. Moreover there is a fair chance of crossing an adherent sub-

One thing I wish to emphasize most strongly, that in petrositis uncomplicated by meningitis, sulphonamide treatment is not only absolutely useless, it is abominably dangerous. It is useless because the drug cannot reach the organisms, it is dangerous because it masks the symptoms and because it may, by useless over-dosage make it impossible to give the heavy doses which may be needed later if meningitis should develop.

In conclusion, may I express my deep gratitude to my colleagues who have so kindly let me see so many of these cases.

Mr. Terence Cawthorne: Meningitis was formerly the commonest cause of death in ear, nose and throat diseases. Courville of Los Angeles, in an analysis of 15,000 post-mortems, found 337 cases of septic meningitis, that is to say, meningitis due to organisms other than tubercle bacillus and meningococcus; of these 175 were otogenic. Whilst the mortality rate of meningitis has been dramatically reduced since the introduction of the sulphonamides it may still be the commonest cause of death.

The basis of any study of otogenic meningitis should be a consideration of the pathways by which infection may spread from the ear to the meninges, because an appreciation of these methods of spread is the key to the whole situation from the surgical point of view.

It will be convenient to consider the spread of infection from the ear to the meninges under three main headings: (a) preformed spaces; (b) vascular channels; and (c) direct spread through diseased bone.

Preformed spaces.—These can be preformed by Nature, by injury or by operation. There are many natural spaces in the temporal bone through which infection can travel, and the petro-squamosal suture when patent and the various labyrinthine channels deserve particular mention. Injury to the skull may open up a channel between the subarachnoid space and the outside via the ear through which infection can enter if proper precautions are not taken.

Mastoid cavities, particularly if the dura has been exposed, can sometimes be a way by which infection spreads, particularly if the dura has been roughly handled. I remember a case in which I did an extensive operation of the Neumann type for streptococcal meningitis secondary to ear disease. About a year later this patient developed a severe upper respiratory infection, and within twelve hours she was delirious. The cerebrospinal fluid was found to be teeming with pneumococci and the infection had clearly rushed through the upper respiratory tract to the mastoid cavity with its widely exposed dura. She recovered from this second infection.

A characteristic feature of this spread by preformed spaces is that the meningitis appears within a matter of hours.

Vascular channels.—The second group in which infection may spread from the infected middle-ear cleft to the meninges consists of those in whom the spread is by vascular channels. I do not necessarily mean the lateral sinus or any of the large blood-vessels, but would include the small veins. There are many intimate connexions between the venous drainage of the temporal bone and the meninges, and spread in this way probably accounts for those cases of meningitis which occur within a few days of the original otitis media.

Bone destruction.—We are all familiar with the patient with an otitis media who develops meningitis, either before or after a mastoid operation, perhaps two or three or more weeks after the otitis media. This third group, of course, consists of those to which Mr. Watkyn-Thomas has just referred. I do not think as a rule they occur within less than two weeks from the primary infection.

Then there are the cases of long-standing otitis media which give rise to meningitis. In a way these belong to the group of cases arising from preformed spaces, because the disease may have been slowly eroding the bony boundaries of the middle-ear cleft for years, resulting in an exposed dura and the patient at the mercy of any upper respiratory infection.

Thus meningitis appearing within *hours* of the primary aural infection is likely to have travelled by preformed spaces; within *days* by vascular channels; and within *weeks* or longer by bone destruction.

Nomenclature.—Such tangled verbiage as "sympathetic meningitis", "meningismus", "ménigite de voisinage" and "meningeal reaction" are used to indicate what are all part of one disease, namely meningitis.

I think, therefore, that it is better to call all these cases meningitis and then, when the cerebrospinal fluid has been examined, the qualifying adjective can be added—"serous" if there is only an increase in pressure; "cellular" if there are cells, and if in addition to an increase of cells there are bacteria, it can be called a "bacterial meningitis", at the same time naming the bacterium.

I have mentioned pressure, cells and bacteria only because these are the three essential

features about which information is sought when the cerebrospinal fluid is first examined. At that time or later additional information may be desired such as chlorides, sugar, protein and sulphonamide content.

Certain types of meningitis, especially if they occur following long-standing suppurative otitis media, where the labyrinth has been invaded, show a fairly high proportion of lymphocytes in the fluid, and it may well be that the number of lymphocytes furnishes some idea of how long the infective process has been going on.

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arachnoid space. Secondly, the otologist may with very little trauma and minimal reactionary œdema, tide over the patient, for subsequent drainage or excision, by the simple process of tapping and re-tapping. Thirdly, in a notable minority of cases the neuroglial agglomeration and fibroblastic proliferation will have produced an encapsulation sufficient for minimal surgery and at the same time insufficient mural rigidity to prevent obliteration of the cavity on emptying. Such cases may recover on simple tapping.

There are two cardinal principles in the conduct of the acute phase of brain abscess: (1) Interference should be properly timed; and (2) it should be as little as may be and as gentle as possible.

In labyrinthine invasions, I find chronic otitis media and especially cholesteatomatous lesions a frequent cause of erosion via the lateral and superior canals and less commonly through the promontory. In many cases I have sucked cholesteatoma from the labyrinth and in not a few found that organ virtually absent, though the facial nerve has usually held its own throughout. I am not convinced that this route, in such chronic and resisted lesions of this kind, accounts for more than a small proportion of leptomeningitic cases falling within my experience and it has been my custom simply to deal with the labyrinth secundum artem during the course of operation. Acute purulent labyrinthitis has been a rare disease among my cases, perhaps because conservatism showed so many invasions, apparently catastrophic, to recover some function quite quickly. Acute invasions, however, are clearly to be feared in relation to meningitis because of the preformed paths but it is pertinent to mention that these paths cut both ways, e.g. the frequency of cochlear destruction in meningococcal invasions. I suggest that it is quite possible for an otogenic meningitis to invade a labyrinth via the nerve sheaths, and that scrutiny of most careful kind is necessary before accepting a post-mortem labyrinthitis as necessarily indicating the route of invasion.

If all acute ears were X-rayed, petrositis would be established with a frequency quite out of proportion to its real significance. This is but another example of the need to interpret X-ray shadows by the light of clinical experience. This entity can be recognized quite frequently and indeed one's clinical estimate may often be supported by serial X-rays but I do hold that the important partner is the clinical estimate. Potentially dangerous though the condition may be, it is a fact that a relatively small proportion of cases develop real complications and I believe that the mortality attending unrestrained surgery is a greater danger. The majority of cases will react to a careful mastoidectomy, with an odd case here and there calling for a little investigation of the deep track.

Mr. Eric Watson-Williams said that he was amazed to hear of an abscess being tapped three or four times. His own practice had been, when he had found an abscess, to put in the smallest drain he could. He had had a certain number of recoveries by following that method.

He could not see the object, if there was a dead ear, of leaving the suppuration in the labyrinth undrained. The sulphonamides would do a great deal of good, but not too much must be expected of them. One point of importance to the patient was that if the ampulla were carefully curetted he woke up from the anæsthetic completely recovered from the vertigo. He had had one case in the previous week, and what impressed the patient who had had five days of acute labyrinthitis was that he woke up without any sense of giddiness.

In meningitis, again, the sulphonamides did much, but there were cases in which the meningitis recurred. It was very important to drain—he did not mean through the internal auditory meatus, for that was only very rarely indicated—that is to say, to get proper drainage of the infected focus. Before the days of sulphanilamide he had quite an encouraging number of recoveries simply from early operation, with the giving of intravenous silver in large doses.

Mr. J. N. Deacon referred to two cases of acute mastoiditis, each with meningitis which had developed in spite of heavy dosage of sulphonamide given prior to admission. In each case organisms were found in the C.S.F. and pus in the mastoid. Penicillin 10,000 units in 1% glucose was given intrathecally at the time of the mastoid operation and continued daily. The temperature fell to normal in forty-eight hours, in one case after two injections and in the other after three. They had now had six and seven injections respectively, and were doing remarkably well. He was considering now taking them off penicillin.

Mr. Donald Watson said that he had started the study of labyrinthitis with J. S. Fraser twenty-four years ago and, with his help, learned a great deal about it. After two years there he went down to Bradford and carried out the teaching which he had learned in Edinburgh, but in the course of four years in Bradford he had three deaths from meningitis following labyrinthitis. On the other hand his colleague had no deaths from meningitis following labyrinthitis. He discovered that the one respect in which his colleague's practice differed

from his own was that his colleague did not test any labyrinth. He thereupon followed the same course in those cases where pus was present, and now for eighteen years he had not tested cases with labyrinthine symptoms when infected, and he had had only one death from meningitis which had been preceded by labyrinthitis. That one case was of the fulminating type mentioned by Mr. Watkyn-Thomas in which the mastoid labyrinth and the meninges were all infected, in a child of 6. This had been a negative kind of research, but he would make a plea that any case of labyrinthitis should be treated very conservatively and rested, and then, when the symptoms had disappeared, one could use one's surgical judgment to do what was thought to be required.

Major E. P. Fowler, Jr., U.S.A.M.C., said that in an analysis of anatomical specimens the commonest site of invasion of the meninges was through the wall of the posterior fossa. The invasion was directly through the back of the petrous bone and, most commonly, through a cell which was very close to the anterior wall of the internal auditory meatus.

He thought that surgery was necessary with meningitis, though he agreed that it was not important to carry it out as quickly as they used to do. Infection in the temporal bone should be drained. However, if one operated on a mastoid too soon it was likely to spread. On the other hand, the making of a small hole into the mastoid would relieve the pain and give adequate drainage when myringotomy was inadequate. It was a very simple procedure to increase the drainage in this way and not dangerous. With sulphonamide therapy it was sometimes unnecessary to do a complete mastoidectomy at a later date but this was not the rule.

Colonel Norton Canfield, U.S.A.M.C., said that for several years past at his hospital they had worked on their brain abscess cases in conjunction with the neurosurgeons. The location for the drainage had been a source of considerable discussion as to whether it should be through the mastoid or through a posterior incision entirely outside the field of mastoid operation. If the brain abscess were given time enough to become encapsulated the results seemed to be better with the draining of the abscess by a second incision over the abscess site, not through the mastoid wound. He had no figures at the present time to bear that out, but it seemed that the handling of the dura and the brain substance itself, with the wide drainage of the abscess which could be done in that manner—and could be done by the otologist if he was able to handle brain tissue—gave better results in these cases.

He wanted to emphasize again the point concerning the testing of the labyrinth by stimulation in the presence of infection. He had not carried out that procedure because of the possibility of increasing the intratemporal bone pressure. He wondered whether Mr. Watkyn-Thomas had found cases in which it had been followed by a severe reaction.

Another way of cold caloric stimulation of the labyrinth in the presence of pus was to use air and it would then be possible to decrease the temperature without the disadvantage of introducing cold water.

Mr. Cawthorne's presentation had opened up a good many points which might be discussed. He was of opinion that the fulminating cases which occurred in certain patients belonged to a group in which the middle ear and temporal bones constituted only a portion of the entire picture, and it was not necessarily the fact that the meningitis made its appearance in the meninges by means of or through the ear. To give such cases a sulphonamide drug was one of the greatest protective measures at their command.

Mr. W. Stirk Adams described a case under the care of his colleague Dr. J. M. Smellie, in the General Hospital, Birmingham, some years ago, which supported the suggestion, raised during the discussion, that caloric tests carried out in the presence of labyrinthitis prejudiced the recovery of the patient.

The patient was a young man in the early twenties who was admitted to hospital for investigation of a left facial paralysis. His history was that six years previously a paresis of the left side of his face appeared after taking part in a cycle track race. The paresis disappeared within twenty-four hours, but recurred after every race, at first disappearing rapidly, but in the course of time taking longer to recover. He gave up racing for this reason some eighteen months before admission, but his facial paralysis did not recover and persisted unchanged until his admission for investigation.

General and neurological examination was negative apart from the paralysis of his left facial muscles, and deafness in his left ear. In this he was only able to hear a whisper at 1 in. distance. His left drumhead was intact, retracted, and almost immobile. Caloric tests were carried out to ascertain whether his labyrinthine function was affected. The evidence of the labyrinth tests and the presence of residual hearing proved a live labyrinth.

Within twenty-four hours of this caloric test the patient developed headache, a positive Kernig and neck rigidity; lumbar puncture obtained a C.S.F. containing several thousand

cells per c.mm. Though the condition appeared to be of great gravity he made a rapid and uninterrupted spontaneous recovery, and within a few days the storm was past.

Shortly afterwards Mr. Stirk Adams explored his left mastoid which had been shown to be sclerotic by X-ray. The bone was eburnated and the lining membrane in the mastoid antrum and air cells was thickened. No exudate was present, and there was no cholesteatoma. Bone was removed to allow examination of the middle and posterior fossa and dura. No extradural abscess was present. He made an uninterrupted recovery from the operation.

The speaker said it was clear that the meningeal reaction (meningitis aseptica) was produced by the use of the caloric tests in an ear which was the site of a chronic low-grade infection with an intact drumhead.

The President remarked on the diminishing number of complications such as brain abscess, meningitis or labyrinthitis. Where they saw ten cases in the old days they did not see more than one to-day. It was therefore more and more important that they should have clear-cut views as to how these cases should be treated when they did appear.

Concerning brain abscess his own viewpoint was rather altered from the time when, in consultation with a neurosurgeon, he was asked to say whether a brain abscess in the temporosphenoidal lobe was of aural origin. He gave the opinion that it was and intimated that an operation on the ear was desirable. That, however, was not first proceeded with, for the neurosurgeon decided to open the abscess through an osteoplastic flap in the temporal region. Later on he was asked to carry out the radical mastoid operation, with the result that the patient was still alive and perfectly cured.

That episode rather made him wonder whether they should always consult a neurosurgeon in these cases or not. He came to the conclusion that it was not always necessary, especially in those cases where the diseased track leading down to a rather superficial abscess was found in the first instance, and at the mastoid operation. It was his practice to drain brain abscesses with rubber tubes; he had never resorted to aspiration. His cases had been few, but he had achieved successful results by putting in a tube and treating it carefully so as to disturb the surrounding parts as little as possible. On the other hand in cases where one was not quite certain of the track a neurosurgeon should be consulted.

Mr. E. D. D. Davis said, in reply to Mr. Watson-Williams, that the results obtained by the otologist were very much better than by the neurosurgeon. The otologist should be a general surgeon with a sound knowledge of neurosurgery and otology.

Neumann attributed his good results—47%—to the fact that he made an early diagnosis before the presence of naming aphasia. The acute or subacute abscess might be fatal before the abscess was encapsuled. He supported Major Fowler when he said that the large majority of cases of otitic meningitis arose in the posterior fossa of the skull.

Mr. F. W. Watkyn-Thomas said that he was glad to have so much support for his view about petrositis. He was convinced that the great majority of cases would subside with adequate mastoid operation. It was exceptional to have to carry out an actual operation on the petrous bone. He, too, inclined to the "heresy" that cholesteatoma was not itself infective, but by the time the otologist saw the cholesteatoma it probably was infected. Facial weakness after labyrinthectomy was not common. If a patient had a facial palsy *before* the labyrinth was operated on it complicated the condition considerably. Such palsies were not always recoverable, but from the results of ordinary labyrinth drainage (he was not referring to translabyrinthine drainage through the meatus) he could never remember getting a permanent facial palsy. He had once or twice found a transient weakness.

Major Fowler's suggestion of making a little hole in the mastoid to give relief of pain in fulminating cases was very intriguing. He had been tempted to do it but up to now he had never summoned up the courage.

An interesting point had been raised by Mr. Donald Watson, Colonel Canfield and Mr. Stirk Adams about the possibility of flaring up trouble by a cold caloric test. He supposed it would be possible that just that amount of irritation, the setting up, so to speak, of a wave, however trivial, in the endolymph, might cause enough labyrinthine disturbance to trickle a dose of poison through one of the preformed tracks.

Mr. Terence Cawthorne did not think it was necessary to do the cold caloric test on the affected side though he did not share other speakers' fears of the consequences. As Hallpike, Fitzgerald and himself had shown, it was possible to do the hot and cold caloric on the sound side and to obtain, together with other indications, the required results.

Section of Neurology

President—Air Vice-Marshal C. P. SYMONDS, C.B.

[January 4, 1945]

DISCUSSION ON DIAGNOSIS AND TREATMENT OF CEREBRAL ABSCESS

Mr. Joe Pennybacker: For the purpose of this discussion I have analysed 50 consecutive cases of cerebral abscess which have been treated in the Nuffield Department of Surgery during the last six and a half years. I have included only those cases in which there were abscesses within the substance of the cerebral hemispheres, and thus I propose to say nothing about subdural or extradural abscess, nor about cerebellar abscesses—although as regards treatment the cerebellar abscesses seem to be more of a problem than the cerebral ones.

Some of these cases came from the general medical and surgical wards and from the Ear, Nose and Throat Department of the Radcliffe Infirmary, and the others were referred directly to the department as suffering from increased intracranial pressure. It is thus selected material to some extent, but Table I shows that the ætiology is in general agreement with previously reported series.

TABLE I.—ÆTIOLOGY OF 50 CASES OF CEREBRAL ABSCESS.

	No. of cases	Died
Metastatic: A. Thoracogenic (lung abscess, bronchiectasis, empyema, 9; subacute bacterial endocarditis, 3)	12	11
B. From other sources (boils, carbuncles, cellulitis, &c.)	6	1
Mastoid infection	12	3
Frontal sinus infection	7	0
Infections of face, scalp, skull, &c.	13	3
Total	50	18

18 cases were due to metastatic infection, the organism being brought to the brain by the blood-stream. These fall into two main groups: those in which the primary infection is in the thorax (12 cases), and those due to sepsis in some other part of the body (6 cases). As in each group the organism is carried by the blood, the division may seem somewhat artificial but the striking difference in the mortality shows that the problem is different in the two groups. Only one of the thoracogenic group recovered, whereas only one of the other group died. The difference is to be found in the pathogenesis of these abscesses: with lung abscess, bronchiectasis, chronic empyema, the cerebral infection is usually a terminal complication of a continuing septic process; whereas in the other group, the cerebral abscess results from a boil or carbuncle, or some other relatively innocent infection which has usually resolved completely by the time the brain abscess demands treatment. Dealing with such abscesses is really more a problem of an unresolved sequel. Furthermore they are usually single, whereas all too frequently the thoracogenic abscesses are multiple, being scattered widely throughout the brain. The only patient in this series who recovered from a thoracogenic abscess was a middle-aged man who developed a lung abscess after an operation for a perforated peptic ulcer. The lung abscess discharged into a bronchus, its contents were coughed up, and the pulmonary infection resolved. Two or three months later he began to suffer from focal motor attacks down the right side of the body and from symptoms of increasing intracranial pressure. He was admitted about three months after the onset of intracranial symptoms, with papilloedema, an incomplete right hemiplegia, and a mild nominal aphasia. A ventriculogram revealed a single lesion in the left Rolandic region and at operation a tough encapsulated abscess mass was dissected out. On section it proved to contain two or three small abscess cavities, although the main mass was perfectly discrete and circumscribed.

The problem of the thoracogenic abscess is well illustrated in another case in which the outcome might have been different had it been possible to arrest the chest infection at a stage when the cerebral abscess was under control.

A man, aged 29, was admitted on November 28, 1941, with a left hemiplegia of one week's duration. He had been in good health until five months before admission when he had lobar pneumonia followed by a left empyema thoracis. This was treated by aspiration and drainage through a rib resection, and the wound continued to discharge copiously up until the time of admission. On November 21, a week before he was admitted to the Radcliffe Infirmary, he had two generalized convulsions, and two days

later a succession of Jacksonian attacks down the left side of the body resulted in a practically complete hemiplegia. On admission, he was markedly wasted, but he was fairly alert, and he complained only of the left-sided paralysis. There were no signs of increased intracranial pressure: the optic fundi were normal and the spinal fluid pressure was 150 mm. There was complete paralysis of the left upper limb, marked weakness of the left side of the face, and to a less extent of the left lower limb. There was also a slight sensory deficit down the left side of the body, but no defect in the visual fields. The spinal fluid contained 6 cells and 55 mg. protein. A ventriculogram on December 1 revealed a slight displacement of the ventricular system to the left side, and this was taken to indicate an abscess in the right hemisphere. In the ensuing fortnight, he complained of more headache and he became progressively more drowsy until by December 16 he was almost comatose. On this day, a burr hole was made in the right frontal region and 6 c.c. of pus were aspirated from the posterior part of the frontal lobe. A small amount (1.5 c.c.) of thorotrast was instilled into the abscess cavity for subsequent radiographic study (see p. 7). He improved considerably as a result of the aspiration, in that he recovered consciousness, had less headache and was swallowing and speaking normally. The improvement was short-lived however. After three days, on December 19, recurrence of stupor indicated that the abscess was again under tension. On this day, an osteoplastic flap was reflected over the abscess and the dura was opened. The abscess could be seen approaching the surface of the brain in the Rolandic area, and a small quantity of pus (2 c.c.) was aspirated from one loculus. The dura was left open and the uncovered cortex was protected by a sheet of gutta-percha laid over the dura. The bone flap was replaced and the scalp sutured firmly. This decompression brought about immediate relief as had the aspiration. The wound healed normally and the sutures were removed on the third day. The need for the decompression was shown by the fact that the flap began to bulge, and X-rays showed that the abscess outlined by thorotrast was being displaced into the decompression opening.

By January 8, 1942, the decompression was bulging so much that the scar was thinned almost to translucence and there were fears that it would burst. The pressure could be relieved temporarily by lumbar puncture, but it was felt that the abscess was now between six and seven weeks old and that it might have a thick enough wall to allow extirpation. Accordingly, on this day, the flap was re-elevated, and a large multilocular abscess was dissected out intact. It weighed 120 grammes. Convalescence was uneventful: the wound healed and the stitches were removed on the third day, when the spinal fluid pressure was 120 mm., the fluid clear and slightly yellow, containing 25 mg. protein and four cells. In the ensuing few days, the decompression area was indrawn, and the patient was quite well in himself, although there had been no improvement in the hemiplegia. The chest wound was still discharging.

On January 25, 1942, it was noted that he was a little drowsy and when he was roused it was evident that he had a slight expressive aphasia. In the following week, he developed a progressive weakness of the right side of the face and right upper limb, and the aphasia became more pronounced. The right-sided decompression area was bulging slightly, and the spinal fluid pressure was 190 mm. The fluid contained 90 mg. protein and three cells. A ventriculogram on February 3 revealed dilatation of the right ventricle, and displacement of the whole system to the right side. The left temporal horn was obliterated and it was evident that there was another abscess in the left temporal lobe. A burr hole was made over it and 8 c.c. of pus were aspirated from the temporal lobe, with the instillation of 2 c.c. thorotrast. This brought about very little improvement, either in his general condition or in the focal signs, so on February 5 a left lateral osteoplastic flap was reflected over the abscess. As in dealing with the right hemisphere abscess, the dura was opened and the cortex protected by a sheet of gutta-percha. The wound healed and there was some improvement in his general condition (state of consciousness, swallowing, sphincter control) but he was left with a bilateral hemiplegia and a profound global aphasia. It was questionable whether there was much to be said for prolonging life in the face of such gross disabilities, but having gone so far, and being uncertain how much of the left hemisphere dysfunction was due to pressure as opposed to destruction, we decided to remove this abscess. The flap was re-elevated on March 9, when it was estimated that the abscess was about six weeks old, and a multilocular abscess was dissected intact out of the left temporal lobe. It weighed 117 grammes. The wound healed, but there was no improvement in his general condition or in the focal signs. On March 23, he was moribund and the spinal fluid was turbid. The left temporal wound was inflamed and pus was aspirated from beneath the galea. He died two days later.

At the autopsy, there was a large trilobular abscess in the left frontal lobe (which was presumably not present when the last ventriculogram was done six weeks before death), and a recent acute infection of the left temporal operative cavity. The right hemisphere bore only the scar of the abscess which had been excised eleven weeks before death. The abscesses in the left hemisphere had thus begun to develop after the right hemisphere lesion had been dealt with successfully, and if the chest infection could have been arrested before they started, the patient should have recovered.

At present then it seems that the only thoracogenic abscesses which are likely to respond favourably to surgical treatment are those in which the chest infection has resolved or is resolving—otherwise the problem is very similar to dealing with intracranial metastases from a malignant tumour of the lung.

Mastoid infection accounted for 12 cases and frontal sinusitis for 7. In Evans' (1931) series of 194 abscesses encountered in the autopsy room at the London Hospital, 62% were due to infections of the mastoid and paranasal sinuses. This included cerebellar abscesses too, and a correction for this series would raise the incidence from 38% to 48%.

As Evans' cases largely occurred in the pre-sulphonamide era, there may be grounds for some encouragement in the difference of 14%.

The fourth group is a miscellaneous one including abscesses due to infected compound fractures of the skull, infected scalp wounds, penetrating wounds, infections of the face, and cavernous sinus thrombosis. They fall into one group because they are infections by continuity as opposed to blood-borne ones. Indeed the mastoid and frontal sinus abscesses fall naturally into this group, but I have put them apart for simplicity in the discussion.

I shall give a brief account of the conditions which may be mistaken for brain abscess and describe the methods in current use for diagnosis.

Differential diagnosis of cerebral abscess.—(1) From other expanding lesions (brain tumours, subdural hæmatoma, &c.). (2) From intracranial venous obstruction ("otitic hydrocephalus", cerebral thrombophlebitis, traumatic sinus thrombosis). (3) From other intracranial infections (leptomeningitis, extradural abscess, subdural abscess, tuberculous meningitis). (4) Arterial hypertension. (5) Psychoneurosis.

In a neurosurgical clinic it is natural that the differentiation from other space-occupying lesions should be the most common problem. If intracranial symptoms occur during any of the infections mentioned above, the diagnosis of cerebral abscess is not likely to be missed. It is in those cases in which the primary infection is not obvious that the greatest difficulty arises: the subject with mild chronic bronchiectasis who does not know that he has anything more than a touch of bronchitis, or the patient who has a crop of boils which clear up and leave him in good health so that he forgets to mention the boils when he is being investigated for cerebral symptoms, or the patient with a more trivial and obscure infection which may cause little or no local constitutional disturbance, even though some organisms have gained the blood-stream, and been carried to the brain where an abscess begins to develop while the primary source is resolving. These patients present themselves for treatment with symptoms and signs of a progressive intracranial lesion. In addition to the signs of increased pressure, there may be focal neurological abnormalities depending on the site of the abscess. But the clinical state may differ in no important respect from that produced by other expanding lesions, such as neoplasms and subdural hæmatoma. The clinical signs of infection are not of much help: the temperature is no sure index, as it may be normal throughout the course of a brain abscess; the pulse-rate, respiration, and state of consciousness vary with the degree of intracranial pressure and the variations are similar to those met with in other expanding lesions. What additional aids have we?

The examination of the cerebrospinal fluid is perhaps the most important single one. In over 90% of cases in this series the fluid was abnormal, and of positive help in diagnosis. The significant change is a slight increase in the protein and cell content. Both may be increased or in some cases, only one; thus in 17 cases the protein content was normal but in all except two of these the cell count was significantly raised. The pleocytosis is usually a slight one however. In 70% of cases, the cell count ranged between 5 and 50 per c.mm. Higher counts were met with in some cases of acute abscesses and in the phases of clinical meningitis which may occur during the incubation or treatment of a brain abscess. Although these changes in the spinal fluid are so constant, they are by no means pathognomonic of brain abscess. Increase in the protein content is a very common finding in cases of intracranial neoplasms of all sorts, and the cell count may be raised with or without an increase in the protein content. Some cases of degenerating and necrotic gliomata situated near the ventricular system or the subarachnoid space may show a marked pleocytosis, contributed to by polymorphs as well as by lymphocytes, and in these cases the short history of a progressive intracranial lesion may make the differentiation from an abscess difficult or impossible. Furthermore in a small minority of cases, the spinal fluid may be quite normal in cases of brain abscess, and a normal fluid should not be taken as excluding an abscess.

Routine X-rays of the skull should always be taken; they may show a penetration of the skull in what has been regarded as a trivial scalp wound. In such a case, a child was watching his father chop wood when he was struck by a flying splinter, and there was a graze at the hair line in the left frontal region. The wound did not bleed, and the child was not dazed or unconscious and nothing was thought of the injury at the time. On the following day, he came home from school, complaining of not feeling well, and that evening he had a generalized fit, the first in his life, and was brought to hospital. He recovered consciousness after about an hour, and on the following day seemed to be perfectly well, but X-rays of the skull had shown that there was a penetrating wound of the skull just beneath what appeared to be a scratch at the site of injury, and he subsequently developed a large bilocular abscess in the frontal lobe. X-rays may also show a calcified neoplasm in a case suspected of having an abscess.

and thus clear up the diagnosis. Shift of the pineal gland may indicate an expanding lesion in one or other hemisphere, and this information may be of value in some cases. The only positive evidence of abscess formation from X-rays alone is found in the rare cases of gas-formation in the abscess. I have not encountered this myself, but there are several reports in literature.

Routine X-rays of the chest may reveal undiagnosed bronchiectasis, lung abscess or, alternatively, a neoplasm, and this too is valuable information.

Even with these considerable aids, we are often left in doubt as to the presence of an expanding lesion, its site and nature. Ventriculography usually answers the first two questions, i.e. as to whether or not there is an expanding lesion, and, if so, its site. It usually tells us little or nothing about the pathology of the lesion, and in our clinic we rely strongly on exploratory aspiration. Knowing the site of a lesion, a burr hole is placed over it and a brain needle is introduced. If it is a neoplasm, various degrees of resistance are met and in about 90% of cases there is sufficient tissue in the eye of the needle for a rapid examination with toluidine blue, as described by Dudgeon and Patrick (1927), and developed especially for the nervous system by Russell *et al.* (1936). If the lesion is an abscess, pus will be recovered, and the burr hole is suitably placed for further treatment. This procedure will also disclose a subdural hæmatoma, extra- or subdural abscesses, and the small incision used for the burr hole does not interfere with any other large incisions which may be necessary to deal with the lesion definitely.

In some cases the exploratory aspirations may need to be undertaken rather blindly: the patient may be too ill, or time may be too precious to warrant a ventriculogram; or the ventriculogram may have failed to fill the ventricle on the affected side, and all we know as a result of this investigation is that there is a lesion in one or other cerebral hemisphere. This is always unsatisfactory, but by piecing together the shreds of clinical evidence, it may be possible to say whether the aspirations should be made in the frontal, temporal or occipital regions. In some cases three or four burr holes have been made before the lesion has been found.

There is one diagnostic method which has not been widely enough employed in this country and that is angiography. The injection of thorotrast into the internal or common carotid artery seems to be an innocuous procedure, and it shows very clearly the site of the lesion. The absence of blood-vessels at the site of a lesion suggests that it is either an abscess or a cystic neoplasm, and in either case an exploratory aspiration would be made. Arteriography has the advantage that it does not upset the patient to the same extent that ventriculography does, as it usually does not alter the intracranial dynamics at all. It has the disadvantage that the findings are often more difficult to interpret, even in the hands of experts, and that it cannot be repeated with the ease of ventriculography. As an example of the difficulty of interpretation, I should mention the case of a middle-aged woman who had had chronic mastoiditis for some years before she ultimately had a flare-up which led to a radical operation. During her convalescence, she complained of rather more headache than is common, was often noticed to be drowsy, and a trace of nominal aphasia was detected. It was a right-sided mastoid infection, but she was left-handed and the language function was probably represented in the right hemisphere. As time went on she developed papilloedema, a slight defect in the upper quadrant of the opposite homonymous field of vision, and slight weakness down the left side of the body. The spinal fluid was under increased pressure, and the changes were consistent with abscess formation. An arteriogram lent further weight to this diagnosis and a burr hole was made over the right external meatus. At a depth of 2 cm. from the dura, a faint resistance was met, but no pus could be aspirated. There was some tissue in the eye of the needle which Dr. Dorothy Russell reported as inflammatory, probably granulomatous. We thought that there were probably small pyogenic abscesses which had not yet formed a discrete mass, and decided to keep her under observation. As time went on her symptoms and signs became more marked, and it was clear that something else would have to be done. We accordingly reopened the burr hole, and on this occasion, some eight weeks after the first attempt, a dense resistance was met. We thought that this was an encapsulated abscess and that the time had come to take it out. This was done. An ovoid mass was excised from the inferior temporal region, adherent to the dura over the tegmen tympani. The surrounding brain looked normal. When the mass was examined histologically it proved to be a tuberculoma. The mastoid infection had been a tuberculous one all along, but this was not known until after the pathology of the intracranial extension was established.

These are general observations which apply to abscesses in various parts of the brain and of various origins. There are two special sites, with special problems which I should mention before passing on to the other aspects of differential diagnosis.

Mastoid disease accounted for 24% of the cases in this series. Although this incidence

is rather less than is usually reported, they form a sufficiently large group to deserve special mention. An abscess may begin at any stage of the mastoid infection. We have had some cases of temporal abscess which have occurred after an acute otitis media which has resolved or responded to treatment in ten days or a fortnight and the mastoid infection has caused no further trouble despite the continued development of the abscess in the temporal lobe. More commonly the intracranial extension begins during a flare-up of chronic mastoiditis and in some cases the first symptoms occur after operation for the mastoid infection.

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cerebral veins. In both, the spinal fluid pressure is elevated, but usually not to the critical heights which obtain with abscesses or neoplasms. The fluid is usually normal on analysis. But there are often slight abnormalities which may leave the diagnosis in doubt and the only way to be certain is to do a ventriculogram. In the cases of sinus obstruction, the ventricular system is usually normal, while in the cases of cerebral thrombophlebitis, the affected ventricle may be a little smaller than its fellow, but there is no local deformity or displacement such as would be expected from an abscess. In some cases of cerebral thrombophlebitis, the affected ventricle may be quite collapsed, and the system markedly pushed over to the opposite side—in such a case the mode of onset, i.e. its rapidity, favours a thrombotic lesion rather than an abscess, but most surgeons will prefer to put in an exploring needle at various sites to be certain that an abscess is not being missed.

The differentiation from other intracranial infections is often extremely difficult. Examination of the spinal fluid may tell about an acute pyogenic meningitis or tuberculous meningitis, but I know of no certain way of diagnosing a subdural or extradural collection as against an intracerebral one. Indeed one or the other may coexist with a brain abscess, and it is our practice to make burr holes at two or three places to see what is going on.

I find that there have been 7 or 8 cases of arterial hypertension which have been sent into hospital suspected of having brain abscesses. These were patients with chronic mastoid or frontal sinus infections, who complained of severe headache of a type very similar to that due to increased intracranial pressure. The general practitioner had discovered striking changes in the fundi, but these changes were those of an arteriopathic retinitis, and the headache was due to arterial hypertension. The spinal fluid is normal in these cases, and there are usually no focal neurological abnormalities. If there is any reasonable ground for doubt a ventriculogram settles the matter at once.

I mention neurosis in the diagnosis because there are a group of patients with chronic mastoid or sinus infection who go on complaining of persistent headache for a period of months or years and sooner or later either the patient or his doctor suspects that this headache must be due to an abscess. In such cases, there are no focal signs, the spinal fluid is normal, but again it may take an air-injection to satisfy the patient or his doctor that there is no abscess.

I hope that I have not made the matter of diagnosis appear too simple because even with all the additional aids at our disposal, and with the possibility of an abscess well in our minds, there are mistakes: cases suspected of having abscesses turn out to have tumours, and in two cases in this series, the presence of an abscess was not disclosed until the autopsy. One case was that of a man with multiple cerebral and cerebellar abscesses in which we thought the condition was due to tuberculous meningitis because of the diffuseness of the neurological signs and the fact that the spinal fluid chlorides diminished progressively to a level of 570 mg.%. The other was a child who was admitted with a pneumococcal pyocephalus which proved fatal. At the autopsy, the pyocephalus was shown to be due to a small frontal abscess leaking into the ventricle. This case was instructive because a ventriculogram was done, and it revealed symmetrically dilated ventricles without displacement which we thought excluded an abscess in either hemisphere. Further study of the ventriculograms revealed a small dent in the inferior surface of the right frontal horn, corresponding to the abscess in the inferior part of the frontal lobe which had ruptured into the ventricle. The infection in this case arose from a bean having been lodged in the nostril three years before the onset of the pyocephalus.

Treatment.—There are two factors which cause death in cases of cerebral abscess: first, a spread of the infection to the ventricular system or to the subarachnoid space, causing a diffuse infection of the nervous system; and, secondly, increased intracranial pressure due to the size of the abscess and the oedema associated with it. Treatment must thus be concerned with both of these factors. In dealing with the first, we have powerful allies now in the sulfa drugs and penicillin, and the time may come when the mortality of brain abscess is largely determined by the sensitivity of the causative organisms to the various chemotherapeutic agents.

Most surgical procedures are directed to drainage of the abscess, with the immediate purpose of reducing intracranial pressure and lessening the risk of rupture of the abscess into the ventricular or subarachnoid systems. Various methods have been employed: drainage by tubes, open drainage on to the surface by uncapping the abscess and allowing a fungus to form, marsupialization, &c. We have abandoned tube drainage because of a considerable and unsatisfactory experience in the past. In a previous series, of 17 cases treated in this way only 4 recovered. Table II shows the methods which have been employed in this series.

TABLE II.—METHODS OF TREATMENT.

I. Simple aspiration ...	No. of cases	Deaths
II. Tube drainage	...	7 (5 bronchogenic; 1 subdural and temporal lobe abscess due to mastoid infection; 1 due to infected scalp wound)
III. Open drainage (fungus method)	...	1 (Bronchogenic)
IV. Aspiration + decompression	...	3 (Bronchogenic)
V. Extirpation	...	2 (1 due to infective endocarditis; 1 due to infected compound fracture)
(Primary extirpation, 7; extirpation after aspirations, 11; extirpation after aspirations + decompression, 8)	26	2 (1 multiple bronchogenic abscesses in both hemispheres (pp. 1 and 2); 1 temporal lobe abscess due to mastoid infection: meningitis after primary extirpation)
VI. Undiagnosed or untreated	...	3 (2 cases referred to on p. 6; 1 due to infective endocarditis)
Total	50	18

These methods have not been employed impartially as in each case we have started with the idea of ultimately extirpating the abscess. This means of course that the patient must be kept alive until the abscess has a wall of sufficient thickness to enable it to be dissected out. This degree of encapsulation takes from five to seven weeks from the onset of the infection, as gauged from the cases in which it has been possible to assess the age of the abscess with accuracy. As a principle of treatment extirpation was first advocated by Vincent *et al.* (1937) who showed that it was possible to tide over an acute abscess to the chronic encapsulated stage by aspiration and decompression. Our experience has taught us that the decompression is often unnecessary and that it is usually possible to keep the patient alive by repeated aspirations while the capsule is forming.

In brief, the method is to make a burr hole over the abscess, its location having been determined by a ventriculogram or arteriogram, if that is necessary. In most cases of abscess due to mastoid or frontal sinus infection the diagnosis is certain enough to allow these special investigations to be dispensed with, and the burr hole is made over the external auditory meatus, or just behind the hair-line. The pus is aspirated with a blunt brain needle which enables one to feel the resistance of what capsule has already formed. When all the pus has been aspirated, 2 c.c. of thorotrast are instilled into the abscess cavity without moving the needle. This step was introduced by Kahn (1939) and it has been of great value in the radiographic study of the position and size of the abscess at various times. The effect of the aspiration is observed, and it is usually definite if not dramatic. Within a week or ten days, a recurrence of symptoms, and especially of stupor, demands another aspiration and these are repeated until sufficient time has elapsed to enable one to say that the capsule is tough enough for extirpation. If the aspirations are not sufficient, a decompression may have to be done as well, as advocated by Vincent and as illustrated in the case described on pages 1 and 2. When the time comes to remove the abscess, the operation is much as for the removal of a solid neoplasm from the brain, and usually it presents no special difficulties.

We think that this method is applicable in most cases and we feel more confident about a lesion dealt with in this manner than in any other because the infective area has been removed from the brain. There is no chronic or quiescent cavity left which may light up in the months or years to come and cause further trouble.

There is one special problem of treatment of the abscesses due to mastoid and frontal sinus infection which deserves mention. It is as to the priority of treatment: should the brain abscess or the primary focus be dealt with first? In general, it is a matter of relative urgency as to the life of the patient: if he is on the point of death because of increased intracranial pressure due to the abscess, clearly the abscess demands treatment first. Our practice is to make a burr hole and aspirate the abscess as an emergency measure, and then to ask the aural surgeon to deal with the primary focus when the crisis has been passed and the patient's general condition allows operation. If, on the other hand, a patient is suspected of having or known to have a brain abscess in the presence of mastoid or frontal sinus infection which requires further treatment, but is not acutely ill or in immediate danger from increased intracranial pressure, we advise that the primary focus be dealt with first. The decision is often not easy and calls for close co-operation between the aural surgeon and the neurologist or neurosurgeon.

Although the problems of diagnosis and treatment are so numerous and weighty, a brief survey of the results shows that the mortality of cerebral abscess is being reduced to reasonable proportions: although the over-all mortality in this series was 36%, if the thoracogenic group alone is excluded, there are left 38 cases in which treatment had a

reasonable chance of success; and of these 7 died, a mortality rate of 18%. A study of the results shows too that cerebral abscesses are well worth the time and trouble spent on them. It has been possible to follow the 32 patients who recovered, and 30 of them are leading normal or useful lives or in the case of children are pursuing their education normally. The 2 cases which are left deserve special mention; both were cases of right frontal abscess consequent on frontal sinusitis. The immediate recovery was uneventful and both patients returned to a normal and active life. One died in status epilepticus eighteen months after operation, having had one isolated fit in the interval, and the other died in the same circumstances two and a half years afterwards, having had three fits at long intervals, terminating in a final bout of status. An autopsy was done in one case but there were no abnormalities except a scar in the right frontal lobe at the site of the excision. In the other, no autopsy was done but the spinal fluid was perfectly normal just before death, and it is unlikely that there was any recurrence of the infection. This seems to be a property of the frontal lobe in general. We have had other cases of frontal abscess treated by marsupialization, open drainage, tube drainage, &c., which have been subject to recurrent bouts of status, and it is known to occur in cases of injury too. Three or four years ago in our department, a man died in status who had had a gunshot wound of the right frontal lobe during the last war, and he remained in good health until the onset of status twenty-five years later. At the autopsy there was a metallic foreign body embedded in a scar in the right frontal lobe but no evidence of infection or of increased intracranial pressure.

Epilepsy may thus mar an otherwise good result in cases of brain abscess however treated, and all of these cases should be kept on regular sedative treatment for several years after operation.

I have said nothing about a group of lesions which will be of increasing importance in the next few years, i.e. the abscesses due to gunshot wounds. This is partly a tribute to my colleagues in the Services who have attained such a magnificent record for wound healing in head injuries, and have thus prevented abscess formation. Chronic cases will crop up from time to time for the next few years, but I believe the principles of treatment outlined above are applicable.

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Mr. Terence Cawthorne: Orogenic cerebral abscess.—It is generally estimated that the ear alone is responsible for some 40% of cerebral abscesses, whilst the nose probably accounts for another 10%.

Whilst there is no doubt that the sulphonamides and penicillin have reduced the severity of intracranial complications of otitis media and sinusitis, it is as yet too early to say by how much, if at all, the incidence of complications has been reduced.

It is customary to divide otogenic cerebral abscesses into adjacent and distant, according to their relationship to the infecting ear.

The distant abscesses are fortunately few and on the rare occasions on which they are encountered they place a severe strain on the diagnostic acumen of the clinician. According to Nielsen and Courville the frontal lobe is the most likely distant locus, next the parietal, and then the occipital lobe. The probable route taken by the infection in such cases is via the cerebral anastomotic veins. My own experience is limited to one case in which an abscess was found in the temporal lobe opposite to the infected ear.

However, by far the majority of otogenic abscesses are adjacent, that is to say in the temporal lobe or cerebellum adjoining the infecting ear and the incidence seems to be about 3 temporal to 1 cerebellar.

As with other intracranial infections secondary to otitis media, the spread to the brain may be by preformed spaces, vascular channels, or by direct extension through diseased bone and membranes.

Whilst the natural spaces in the temporal bone offer a wide choice of routes by which infection may spread to the intracranial spaces, it does not seem that this alone is often the pathway except in the case of cerebellar abscesses secondary to a labyrinthine infection. A persistent petro-squamosal suture may rarely be a possible channel by which infection may spread from the middle-ear cleft to the temporal lobe. Spaces opened up by surgery may result in abscess formation either by accidental injury or by deliberate implantation as the result of injudicious exploration of healthy brain tissue through a mastoid or other wound.

Vascular channels, and in particular small veins and the superior petrosal sinus, are the likely route in many abscesses, particularly those in the temporal lobe in which there are layers of bone, intact dura and brain tissue between the abscess and the middle-ear cleft.

These two foregoing routes are most likely to be taken in those abscesses which follow an acute and maybe fleeting aural infection.

The direct spread through diseased bone and membranes is probably the most frequent one and is certainly most likely in cases of long-standing aural infection in which there has been a gradual erosion of the bony boundaries of the middle-ear cleft with exposure, possibly over a period of time, of the dura to infection. It speaks well for the powers of resistance of the tegmen tympani and dura whose combined thickness is not more than that of a visiting card, that little more than one brain abscess is seen in every thousand cases of otitis media. The temporal lobe is easily reached from the middle-ear cleft and the subdural space may become shut off and the infection may then spread to the brain, either directly or in its final stages by small vascular channels.

There is one variety of this abscess which may be commoner than a study of the literature would suggest. I refer to a subdural collection of pus with superficial cortical ulceration. This was first described by Macewen and since then Mygind, and Courville and Nielsen have described the condition.

I have operated on 6 such cases and all presented a similar appearance. The tegmen tympani had been eroded by long-standing disease and the dura was necrotic. In 4 cases a small perforation was noted from which fluid was pumped out with each heart beat. On opening the dura fluid pus was evacuated, revealing an ulceration of the underlying brain tissue, varying in area from 1 to 3 cm. and in depth from a few millimetres to 1 cm. They were all situated on the undersurface of the temporal lobe and all presented symptoms of a temporal lobe abscess, though only one had any pyramidal signs. To all intents and purposes these were intracerebral abscesses but, as will be seen when treatment is to be considered, they should, if possible, be differentiated. A possible clue to this condition was in the accompanying meningeal reaction, because it was noted that the cell count in the cerebrospinal fluid was never less than 100. One case was complicated by the presence of another abscess in the temporal lobe; the others all recovered.

Thus it seems that the spread of infection from the ear by preformed spaces and the vascular route may be along a poorly-marked or even obliterated track. On the other hand, direct spread blazes an unmistakable and often isolated trail.

The diagnosis of brain abscess from the otological aspect may present some difficulty. Now and again a fleeting otitis media is responsible for an abscess which only makes itself apparent some weeks after the ear has cleared up. This is sometimes attributed to the inadequate exhibition of one of the sulphonamides in the early stages of the otitis media.

In at least 80% of cases the causal otitis media is of long duration and the presence of cholesteatoma and bone disease can be inferred from the persistence of foul discharge. Difficulty may arise when the otitis media is bilateral and then a more profuse discharge and greater deafness may be valuable clues as to which is the offending ear. Sometimes the diagnosis is not so easy, as may be seen from the following case.

A young man, aged 21, was first seen in a semi-delirious state with streptococcal meningitis and signs suggesting a left temporal lobe lesion—in particular nominal aphasia. Both ears were equally affected in an acute flare-up of a chronic suppurative process, so it was considered that the left ear was probably the offender. His condition did not permit delay and it was decided to proceed with opening his left ear. Before doing so it was discovered that the patient was completely left-handed. The right mastoid was therefore opened, the dura was normal and so the left mastoid was then opened, revealing a necrotic dura, subdural collection of pus and superficial cortical ulceration. Despite all this the patient recovered. Further questioning afterwards revealed that one of the parents and an elder brother were left-handed, so the patient's left-handedness may have been imitative.

So far I have only seen nominal aphasia in left-sided temporal lobe abscesses.

With regard to the treatment of adjacent brain abscess secondary to ear disease, the first step should be a drainage of the infected ear with inspection of the adjacent dura. If the dura is healthy its integrity in this situation should be respected and any intradural exploration conducted via a separate opening. If the dura is necrotic and the condition already described is present, then all that is required is a good opening through the dura with no encroachment whatever upon the brain tissue.

Blind needling through healthy tissue should not be employed for this type of abscess, and it is in order to avoid such an accident that whenever possible the first step in the treatment of an otogenic cerebral abscess should be an inspection via the mastoid of the dura in the neighbourhood of the tegmen tympani.

If there is definite evidence of a diseased and probably isolated tract between the ear and the abscess, then the abscess can be drained along that tract. If there is no such evidence, then the drainage should be made through a separate approach. However, not every case can be easily separated into either of these groups and such border-line cases call for the combined experience of the neurosurgeon and the otologist. The future otologist should have some instruction in the general principles of neurosurgery, and future neurosurgeons might have some otological experience included as part of their training.

Dr. S. P. Meadows, referring to clinical diagnosis, emphasized the difficulty, in certain cases, of differentiating a cerebral abscess from acute meningitis, and mentioned cases of cerebral abscess admitted to fever hospitals. When the report on the turbid cellular cerebrospinal fluid was returned as sterile on culture and with no reduction in chloride content, a cerebral abscess with meningeal reaction was the probable diagnosis. Intracranial thrombophlebitis could also be confused with abscess, particularly when it followed local infection of the sinuses or head. It seemed possible that in some of these cases intracranial thrombophlebitis was a precursor of abscess formation, and that chemotherapy in the earlier stage might prevent abscess formation, which it had appeared to do in one patient. The speaker mentioned cases of cerebral abscess occurring shortly after an operation for acute appendicitis, and after dental extraction. The latter was of interest in connexion with the cranial nerve palsies, which occasionally occurred after dental extraction, and these, as well as a cerebral abscess, might be due to spreading thrombophlebitis from the tooth socket. Finally, a normal cerebrospinal fluid and negative clinical neurological examination did not necessarily rule out abscess formation in the brain.

Brigadier Hugh Cairns said that he was glad that Mr. Cawthorne had recognized the importance of neurosurgical training for otologists. It was to be hoped that ultimately the treatment of brain abscess secondary to ear and nasal sinus infections could be handed back to the otologist by the neurosurgeon. But it was important to recognize that long and thorough neurosurgical and neurological training was required by anyone who aspired to treat acute abscesses. The cases described by Mr. Pennybacker indicated what a hazardous business the treatment of acute and subacute brain abscess was; the successful results in Mr. Pennybacker's series were only obtained by the closest neurological observation of the patients from day to day, often from hour to hour, and by a complete mastery of neurosurgical techniques. It was often a nice exercise of judgment to decide whether to do a decompression or to rely solely on repeated aspiration, in order to bring the case successfully through to the stage of encapsulation, when the abscess could be removed. In these days anyone undertaking to treat brain abscess should be really expert in the use of ventriculography, and in the use of opaque media for arteriography and injection into abscesses. Facility in the use of these techniques could not be acquired without considerable training.

Abscess secondary to gunshot wound of the brain differed in some respects from the brain abscess of civil life. It was more often clinically latent for long periods. In some cases it did not displace the ventricular system to the opposite side, and thus an abscess of considerable size might be present even though the septum lucidum, as seen by ventriculography, was still in the middle line. The original brain wound resulted in considerable deposition of collagen in and about the wound track, and probably the wounded hemisphere was thus more anchored, less easily displaced, than normal. Removal of brain abscess secondary to gunshot wound was also often more difficult than removal of the abscess of civil life: there was so much scarring in the brain, with scarred tracks leading in various directions and not necessarily towards the abscess. Therefore it was advisable, when operating to remove chronic brain abscess after gunshot wound, to turn a large flap and obtain a wide exposure.

The President remarked that the recovery rate in cases of cerebral abscess appeared to have improved greatly in the hands of neurosurgeons. He believed that the techniques employed by them both for diagnosis and localization, and in treatment were of vital importance. It seemed clear, however, that the aural surgeon would be likely to encounter patients with cerebral abscess or suspected cerebral abscess who were critically ill and the circumstances, therefore, might forbid the collaboration between the aural surgeon and the neurosurgeon which Mr. Cawthorne thought desirable. He (the President) welcomed Brigadier Cairns' suggestion that the aural surgeon of the future should include as a part of his training an apprenticeship in neurosurgery. He thought the necessary technical skill could probably be acquired in a relatively short time by a man who had already had considerable experience of operative surgery. As Brigadier Cairns had indicated the clinical judgment which was at times so important in dealing with these cases could only be learned by experience.

Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[April 6, 1945]

The Force of Expiration as a Sign in Anæsthesia [*Abbreviated*]

By H. J. V. MORTON, M.D., D.A.

CLINICAL anæsthesia has now been studied for a century and since the earliest days of its history attention has been drawn to the changes in respiration which accompany changing depth of anæsthesia. It is convenient to describe these changes which, nowadays, form the basis of accepted and reliable signs, in terms of the rate, rhythm, and amplitude of respiration and of the relative contributions of thoracic muscles and diaphragm during inspiration. One relatively neglected aspect of respiratory activity is the study of the changes which occur in the nature of expiration and particularly the force of expiration during anæsthesia.

Inspiration is an active process depending, chiefly, on the activity of the intercostals and diaphragm. With each inspiratory movement the muscles of the anterior abdominal wall relax sufficiently to provide room for the displaced viscera as the diaphragm descends. "Passive" expiration is effected by a combination of the "elastic recoil" of the thoracic walls and actual muscular control (Keith, 1909). Increasingly "active" expiration involves increasingly powerful contractions of the abdominal muscles. The force of expiration is clearly a very variable quantity. How may this force be measured and what is the significance of changes which occur in it during anæsthesia?

THE FORCE OF EXPIRATION

The maximum expiratory pressure which can be achieved by voluntary effort depends on vital capacity, physique, and physical fitness. Here one may deal with figures well in excess of 100 mm.Hg. Pressures of this high order, naturally, do not occur during anæsthesia, and it is more relevant to inquire what kind of pressure develops when opposition is offered to merely "passive" expiration. I obtained information on this point by repeating on normal conscious subjects experiments similar to those described by Haldane and Mavrogordato (1916) but using an anæsthetic facepiece connected to spirometer and manometer. Fig. 1 shows a fairly typical series of results in one case.

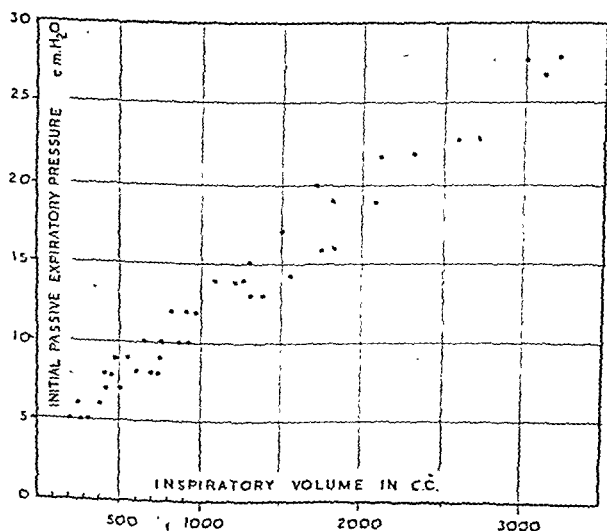


FIG. 1.—Relation between inspiratory volume and initial passive expiratory pressure. (Conscious subject in prone position.)

Clearly, even when expiration is passive, the force of expiration increases proportionately with increasing tidal volume. The larger the volume of air drawn into the lungs the larger the initial expiratory pressure developed. During quiet respiration tidal volume is in the neighbourhood of 500 c.c. Under these conditions I found an average initial

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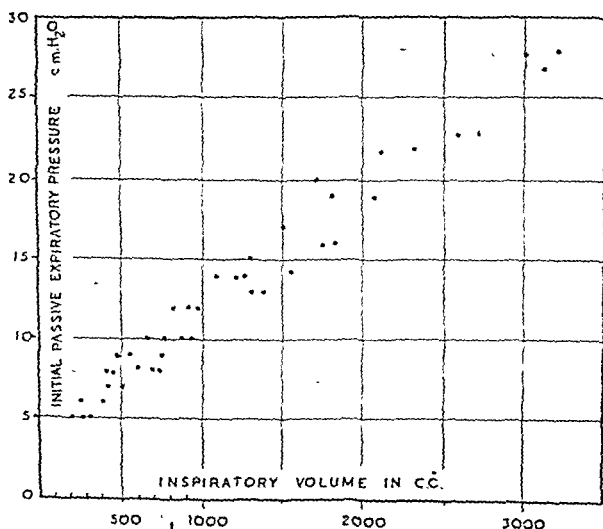


FIG. 1.—Relation between inspiratory volume and initial passive expiratory pressure. (Conscious subject in prone position.)

Clearly, even when expiration is passive, the force of expiration increases proportionately with increasing tidal volume. The larger the volume of air drawn into the lungs the larger the initial expiratory pressure developed. During quiet respiration tidal volume is in the neighbourhood of 500 c.c. Under these conditions I found an average initial

expiratory pressure to be 8 cm. H_2O (5 observations were made on each of 10 normal subjects).

ESTIMATION OF EXPIRATORY FORCE DURING ANÆSTHESIA

With closed circuit methods the problem of assessing expiratory force during anæsthesia is simplified. By palpation of the breathing bag the anæsthetist may obtain a measure of the force and volume of a patient's expirations at any time. When making such a test it is an advantage, for purposes of comparison, to adopt some standard technique. I have found it useful to make a practice of applying a small "basal" positive pressure, comparable to that developed when quiet passive expiration is opposed, i.e. 8 cm. H_2O , by gently squeezing the breathing bag during inspiration, and then holding the fingers fixed in the position the bag occupies when inspiration has reached its maximum. It can then be estimated with one's fingers the force with which the patient exhales against this standard resistance. This manœuvre I have called the Expiratory Pressure Test (E.P.T.).

When making the E.P.T. a manometer connected to the circuit may be found helpful by those unfamiliar with this aspect of anæsthesia. But this is not essential since, after a modicum of practice, significant changes in pressure can readily be appreciated by simple palpation of the bag alone. It must be remembered that even with a manometer one does not measure the absolute expiratory pressure but only some function of it, since the pressure thus recorded is influenced by the patient's tidal volume at the time and the cubic capacity and elasticity of the breathing bag and closed circuit in use.

When using the carbon dioxide absorption technique an absolutely airtight circuit is necessary before making an E.P.T. If a leak occurs not only is it difficult to detect small changes in pressure but unwanted variations in anæsthetic depth will follow replacement of the wasted gases by incorrect concentrations. It is also essential, as always, to work with a perfectly clear airway. Incidentally, while palpating the movements of the breathing bag it is possible to detect minor degrees of respiratory obstruction totally unrecognizable in the ordinary way. The E.P.T. may of course be made when using the semi-closed type of apparatus after momentarily turning off the flow of gases and screwing down the expiratory valve. But naturally the test must be made quickly before carbon dioxide accumulates.

It is both unnecessary and unsafe to produce a high positive pressure when making this test. Untoward results (e.g. mediastinal emphysema, artificial pneumothorax) may follow excessive inflation of the lungs (Marcotte *et al.*, 1940; Adams, 1940; Macklin, 1939). It is seldom necessary to cause a pressure in excess of 16 cm. H_2O and no useful purpose is served by exceeding 18 cm. H_2O in any case. It is difficult to conceive that pressures below this level could cause trouble since this represents no more than the intrapulmonary pressure developed when a normal subject makes a moderate-sized inspiration and holds it.

INFLUENCE OF ANÆSTHESIA ON EXPIRATORY FORCE

Having by now become accustomed to palpating the breathing bag and to noticing changes in expiratory pressure it is pertinent to consider the meaning of these changes. In Table I I have listed the more important factors which may influence the nature of expiration. Now both tidal volume and expiratory "activity" vary with the depth of anæsthesia. Also in any given patient established in the third stage all other relevant factors except operative trauma can be regarded as constants. Since at any particular moment the nature of operative trauma can be observed and taken into account, the force of expiration becomes related to the depth of anæsthesia. In a general way, whether expiration be active or passive, the deeper the anæsthesia the weaker the expiratory pressure and the converse is equally true.

TABLE I.—FACTORS INFLUENCING FORCE OF EXPIRATION DURING ANÆSTHESIA.

(a)	(b) <i>Increased by</i>	(c) <i>Decreased by</i>
General	Good physique. Good health	Poor physique. Debilitating illness.
	Large tidal volume	Pre-operative shock
Premedication	Atropine	Small tidal volume
		Respiratory centre depressants, e.g. opiates, avertin
General anæsthetic agents	Nitrous oxide	Intravenous barbiturates. Cyclopropane
	Light ether	Deep ether
Methods of administration	Any technique favouring carbon dioxide accumulation, e.g. excessive re-breathing, dead space, &c., semi-closed methods	Elimination of dead space. Completely "open" techniques. Efficient absorption. Insufflation
Local anæsthesia		Paralysis of intercostal and/or abdominal muscles by regional, spinal or field blocks
Operative trauma	Sensory nerve stimulation under light anæsthesia	Operative shock. Open pneumothorax

← Vagal traction reflexes →

This may be logical argument but "the subtlety of nature is greater many times over than the subtlety of argument" and to what extent in actual practice can the E.P.T. be used to give a reliable indication of depth in anæsthesia? As the result of observations over a period of years I would say that the greater a patient's expiratory pressure under light anæsthesia the easier is it to assess any subsequent depth of anæsthesia by this sign. Thus a preponderance of the factors appearing on the left side (b) of Table I makes for well-marked differences in the E.P.T. values at different levels of anæsthesia. Under these circumstances the sign is easy both to elicit and to interpret. With a preponderance of the factors on the right side (c) of Table I changes in E.P.T. values will cover a smaller range of pressures and a little practice may be necessary before consistently correct interpretation is achieved. Certainly one occasionally meets abnormal types of response which tempt one to diagnose an abnormal physiological personality, but misleading results are almost invariably due to a non-airtight circuit or failure to take into account the presence or absence of respiratory drives from the operative site.

SPECIAL APPLICATIONS

Cyclopropane anæsthesia.—A patient under cyclopropane shows none of the stimulation of respiration which is a feature of many ether administrations. This is particularly noticeable when depressant premedication has been used. Nevertheless the E.P.T. can be used in the usual way as an aid to maintaining a uniform level of light anæsthesia when spontaneous respiration is adequate.

Under deep cyclopropane it is sometimes the case that spontaneous respiration becomes inadequate or ceases at a time when the degree of muscular relaxation necessary for intra-abdominal operations has not been attained. In these cases it is reasonable to take abdominal relaxation and reflex irritability as guides to subsequent anæsthetic depth. Now when controlled respiration is in progress naturally the E.P.T. cannot be applied. But the anæsthetist can, instead, make a measure of the force necessary to *inflate* the lungs. Although there is, of course, variation between individuals I have found that in lungs using a pressure as low as 8 or 10 cm. H₂O. But I have noticed that in some patients, despite normal thoracic and abdominal movements under light anæsthesia, when respiratory arrest is approached a low pressure may inflate the chest fairly well but may yet produce only a small and delayed diaphragmatic movement. This would imply resistance to downward descent of the diaphragm on account of tonicity of the abdominal wall. Abdominal relaxation in such cases is indifferent. On the other hand inflation causing equal and synchronous movements or preponderatingly diaphragmatic movements is associated with greater abdominal relaxation. In accordance with the general principles already outlined, this "inflation test" is far more reliable if employed whilst surgical trauma is in progress, e.g. it may with advantage be made during the skin incision and approach through the abdominal wall. With increasing muscular tonus lung inflation may be increasingly resisted by the patient irrespective of spontaneous respiratory activity. This resistance is doubtless effected through the Hering Breuer reflex. It has indeed been shown by Adrian (1933) studying vagal action currents in animals that even deep chloroform anæsthesia has no obvious effect on the response to inflation of the end-organs of the lungs.

Thus having taken into account, as always, both the patient's physique and general condition and the possible influence of respiratory drives from the operative site, the resistance offered to inflation of the lungs can be taken as a measure of the depression of reflex irritability, and of anæsthetic depth in terms of abdominal relaxation. This sign is independent of spontaneous inspiratory activity (see fig 2, p. 30).

Spinal block with supplementary cyclopropane anæsthesia.—When a spinal block has been established, of sufficient height to cut off all nervous impulses originating from the site of operation, the chief variable factor which may adversely influence the reliability of the E.P.T., namely operative trauma, is removed. In these circumstances the E.P.T. may confidently be relied on to give an accurate measure of the depth of the supplementary anæsthesia. Guedel (1940) has pointed out that the signs of anæsthesia as employed with other agents are not practical for cyclopropane. This is particularly so in light anæsthesia when the return of the pharyngeal reflex may be troublesome. The E.P.T. simplifies the maintenance of a uniformly light plane. Thus, when too light, the patient may begin to swallow or move his head (let E.P.T. = x cm. H₂O). Half a litre of cyclopropane will restore the *status quo* (let E.P.T. then = $x - 2$ cm. H₂O). Smooth light anæsthesia may then be continued indefinitely by regarding $x - 2$ cm. H₂O as an upper limit in this particular case.

In cases where a spinal block has not completely "insulated" the higher centres from the site of operation reflex effects on respiration may influence the E.P.T. Changes occurring in this way are sudden in onset and are related to operative movements.

On the other hand, E.P.T. changes due to changing depth of anaesthesia take place relatively slowly. Thus, even in the absence of audible reflex effects on the larynx, a sudden increase in the E.P.T. coinciding with manipulation of the stomach will most probably be due to the latter manœuvre. On the other hand a gradually increasing

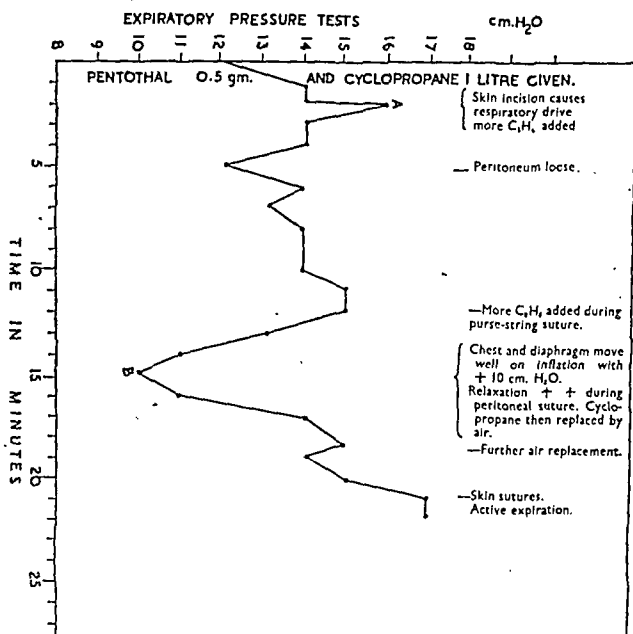


FIG. 2.—Expiratory pressure tests during cyclopropane anaesthesia for appendicectomy.

Female, aged 30. General condition good. Omnipon-scopolamine premedication. CO_2 absorption throughout.

N.B.—Respiratory drive at (A). "Inflation test" at (B).

E.P.T. carried out as described in text.

E.P.T. during the anastomosis stage of a stomach operation will be evidence of lightening anaesthesia (see figs. 3 and 4).

Abdominal operations under general anaesthesia.—Active expiration implies active contraction of the abdominal wall and a "tight" abdomen. Under these circumstances the E.P.T. measures abdominal relaxation. It is a straightforward matter consistently to produce optimum relaxation for the opening of the peritoneum by repeatedly making this test during the approach through the abdominal wall. To take two extreme examples: A patient whose E.P.T. is low or who shows adequate diaphragmatic movement when the lungs are inflated with a low positive pressure, during the skin incision, will also show adequate relaxation. On the other hand, a patient making a powerful expiratory pressure which is increased during the skin incision, i.e. there is a palpable respiratory drive, will without doubt have a tight abdomen unless anaesthesia is rapidly deepened.

It may be asked what constitutes a high or low expiratory pressure? As an example, using ether as the main agent with a 5 litre breathing bag, in a large number of cases I have found that pressures rising from the basal 8 cm. H_2O to over about 16 cm. H_2O indicate an imperfectly relaxed abdomen. Pressures rising from 8 to 12 or less correspond with good relaxation. Now these numbers mean very little for the reasons already given, and there is considerable individual variation. I accordingly advise you to concentrate rather on getting the "feel", both literally and metaphorically, of the changes which occur in any individual patient as anaesthesia becomes deeper and as the abdomen becomes relaxed.

Open ether.—The E.P.T. cannot, of course be made with open anaesthetics, but an appreciation of the changing nature of expiration as previously discussed will be of value to the anaesthetist conducting anaesthesia by the open method. "Open" ether as usually given causes active expiration at the onset of anaesthesia. Careful observation of abdominal movements makes it clear that completely "passive" expiration does not as a rule take place until considerable relaxation has been produced. It is not difficult to imagine the force of expiration corresponding with any particular degree of visible expiratory effort. The inexperienced student giving open ether to an abdominal case should bear in mind that spontaneously active expiration means a tight abdomen. Passive expiration succeeding active expiration, despite surgical trauma, means a relaxed abdomen. In the majority of cases the force of expiration offers the student a progressive sign giving information about anaesthetic depth and abdominal relaxation, irrespective of the nature of inspiratory activity.

The general principles embodied in Table I should always be borne in mind, par-

ticularly when observing expiratory movements. Thus a debilitated patient after opiate premedication and chloroform and ether induction may at the outset of the subsequent open ether maintenance show a low tidal volume and feeble expiratory movements.

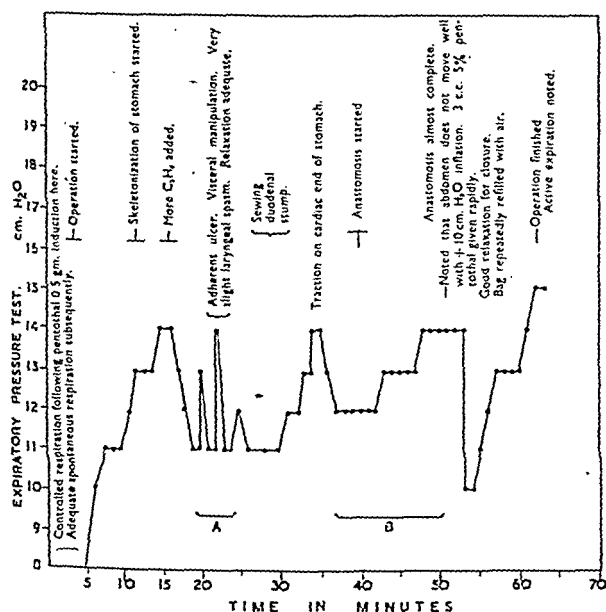


FIG. 3.—Expiratory pressure tests during cyclopropane anaesthesia for partial gastrectomy (ulcer).

Male, aged 58. General condition fair. Omnopon - scopolamine premedication.

N.B.—Sudden irregular changes due to visceral manipulation (A). Gradual increase due to lightening anaesthesia during atraumatic anastomosis stage (B). (Cf. fig. 4.)

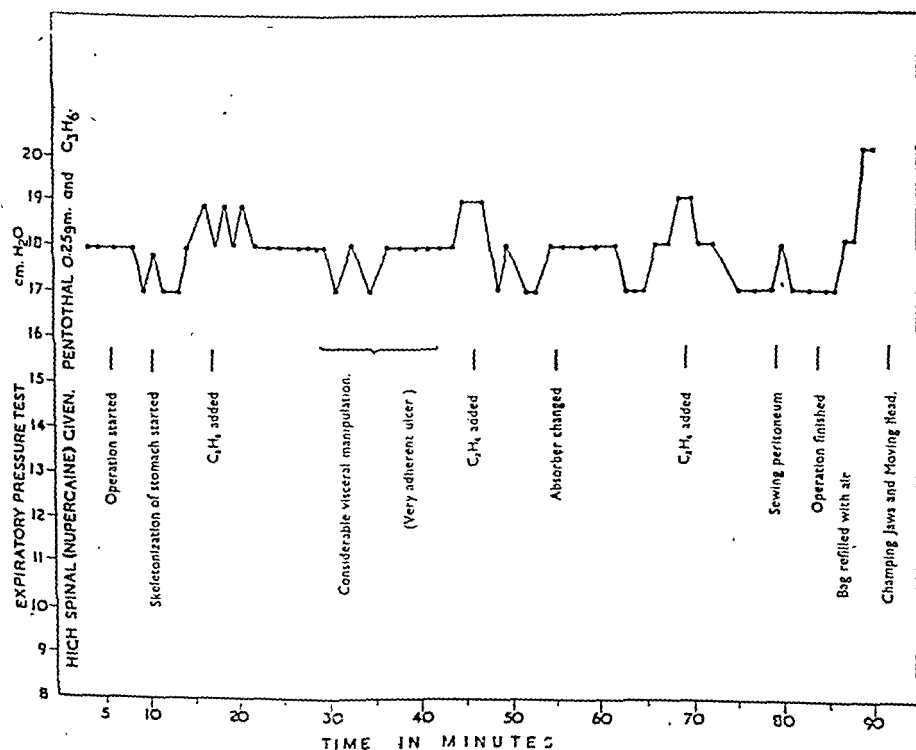


FIG. 4.—Expiratory pressure tests during partial gastrectomy (ulcer). High spinal analgesia. Supplementary light cyclopropane. Male, aged 45. General condition good. Omnopon-scopolamine premedication. N.B.—Absence of respiratory drives. (Cf. fig. 3.) Expiratory pressure test measures depth of supplementary anaesthesia only.

On the other hand, E.P.T. changes due to changing depth of anaesthesia take place relatively slowly. Thus, even in the absence of audible reflex effects on the larynx, a sudden increase in the E.P.T. coinciding with manipulation of the stomach will most probably be due to the latter manoeuvre. On the other hand a gradually increasing

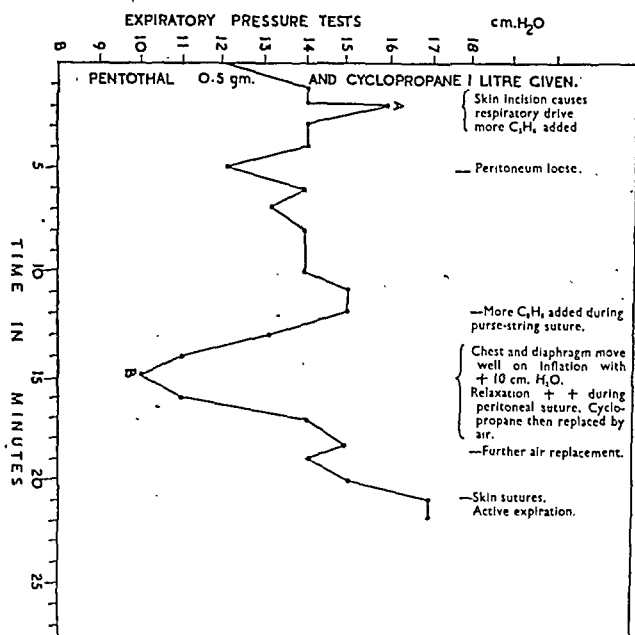


FIG. 2.—Expiratory pressure tests during cyclopropane anaesthesia for appendicectomy.

Female, aged 30. General condition good. Omnopon-scopolamine premedication. CO_2 absorption throughout.

N.B.—Respiratory drive at (A). "Inflation test" at (B).

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[February 23, 1945]

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By Professor ROBERT DEBRÉ, Paris

In 1940 when there was a mass exodus of French people because of the approaching Germans, the children suffered severely from lack of food and shelter. By degrees these people returned to their homes, only to find the food supplies rigidly controlled by the Germans who issued meagre rations for the children. In addition, fuel and light were limited, shoes and clothes wore out and could not be replaced. Fathers were separated from their families by exile, deportation or forced labour in Germany—actually there were 2,600,000 Frenchmen in Germany. French families also suffered because so many of them were in the Resistance Movement—over 115,000 of them were shot and there were hundreds of thousands of political deportees. Many families spent sleepless nights in terror of police raids.

On the question of food supplies, urban districts and regions devoted to some single culture such as wine-growing, suffered the most deprivation because of lack of transport from the richer agricultural areas.

We found that during the war birth-weights were lower; more babies weighed under 6 lb. at birth and far fewer weighed 7 lb. at birth than before the war. In the Parisian district breast-feeding increased from 35% to 90%, so that babies did well for the first six months of their lives. In the poorer suburbs the breast milk was found to be insufficient in calories, the sugar content was normal but proteins were below 13 parts per 1,000 ($N=15$) and fat below 30 parts per 1,000 ($N=35$ to 40). Many of the nursing mothers showed anæmia and slight symptoms of osteomalacia.

For rationing purposes children were divided into four categories $E=0$ to 3 years, $J1=3$ to 6 years, $J2=6$ to 13 years and $J3=13$ to 21 years. E ration was just adequate, i.e. 1,300 calories made up of 140 grammes of sugar, 42 grammes proteins and 42 grammes fats. The milk was scarce and "whole" milk was really skimmed milk. Condensed milk was allowed on a medical certificate but all forms of tinned and powdered milk were scarce.

Those on $J1$ ration (3 to 6 years of age) did not fare too badly; and they also got half a litre of milk per day when it was available. But from 6 to 13 years and 13 to 21 years the ration was inadequate. For instance, in December 1944, a boy of 18 years of age was allowed 1,600 calories although he should receive 2,400 calories per day, 300 grammes of carbohydrates, 21 grammes of vegetable proteins and 6 grammes of animal proteins instead of 30. The calcium in this ration only amounts to 200 mg. per day, one-sixth of what is necessary during this growing age when three-quarters of the skeleton is being built up. Though phosphorus is not so short the calcium-phosphorus ratio is wrong.

The vitamins are just about adequate in this ration—bread containing all the B vitamins, vegetables containing the necessary A vitamins. Vitamin C, however, was often missing owing to the scarcity of citrus fruits.

In January 1945 the shortage of fats and proteins became worse and it was imperative that immediate supplies should be imported by the Allies.

During the four years of German occupation, excepting for several months, children managed to receive their milk—but it was practically impossible for their parents to find for them animal proteins needed for their growth.

This food situation, far from improving after the Liberation, has grown worse: not only is it more difficult to find meat, vegetables, fruits and eggs, but milk to children over 1 year is no longer allowed. The result is that the health of children from 1 to 3 years of age is definitely affected.

Weight: Cayla, Launay and Boulanger-Pillet, for the Seine Bureau of School Health Inspectors, compare the weights of 23,000 children during the first and third terms of 1941 and 1942 with the pre-war averages. 65% of the pupils have put on 2 to 3 pounds whereas before the war they used to put on 3 to 8 pounds; 22.8% have not put on any weight at all; 12% have lost from 1 to 3 lb.

School children from 14 to 18 years of age have mostly lost weight; the heaviest loss in weight has been among the children from 10 to 12 years of age. There is no difference between the sexes.

Correct interpretation of such feeble movements may need experience. Tidal volume alone is not a reliable guide to anæsthetic depth and in this case the student may sadly miss the information which response to inflation of the lungs would provide. On the other hand a vigorous patient premedicated with atropine only and induced with ethyl chloride will probably show powerful expiratory movements in plane I even after a smooth induction. In the latter case, judgment of subsequent depth from changes in visible expiratory effort is simple.

Intrathoracic operations.—When controlled respiration with cyclopropane is in progress the inflation test already referred to may be used as a guide to depth. When some degree of spontaneous respiration is present the usual E.P.T. is particularly useful since the sometimes subtle variations in respiration accompanying the peritoneal and vagal traction reflexes of abdominal surgery do not arise. The only variations in expiratory force and rhythm likely to be met will be due to bronchial or hilar manipulations under light anæsthesia and the connexion between stimulus and response immediately apparent. Thoracic surgery provides opportunity for visual demonstration of the E.P.T. in so far as the movements of the diaphragm during expiration can be actually observed. These visible movements can be conveniently correlated with the palpable expiratory pressures developed in the closed side of the chest, particularly in cases where the mediastinum is relatively fixed.

Operative shock.—As a patient goes into a state of "shock" changes take place which simulate in many ways the changes which occur with deepening anæsthesia. A sudden considerable hæmorrhage will lower the plane of anæsthesia although no increased quantity of anæsthetic agent has been administered. In these circumstances expiratory force will become weaker and the E.P.T. may be used as a means of assessing the patient's debilitation. Following hæmorrhage or shock from other causes anæsthetic concentration should be reduced and by immediately so doing relative overdosage can be avoided. The E.P.T. is of value when adjusting concentrations for this purpose.

Although the length of time a patient takes to "come round" after an operation depends mainly on the length and depth of the anæsthetic and the nature of the agent used the degree of operative shock incurred also plays a part. Other things being equal, muscular tone and reflex irritability increase more rapidly in the fit subject when the anæsthetic agent is removed. The E.P.T. values will be higher in the fit patient than in the shocked one on account of the muscular flaccidity and depressed reflex irritability which are a feature of the latter's condition. A quickly increasing expiratory pressure at the close of an operation implies a good prognosis with regard to the patient's general condition in the immediate post-operative period.

Anæsthetic teaching.—The signs of anæsthesia are of special interest and importance to students. The inexperienced anæsthetist will find the E.P.T. of particular value in cases where the usual signs of anæsthesia are not readily discernible, e.g. when the patient is, from his point of view, completely covered with towels and instruments. The value of observing expiration in cases where the more classical signs are poorly developed has already been mentioned. The beginner who finds difficulty in assessing depth with closed circuit anæsthesia will find this test helpful and he will come to regard the breathing bag as a continuously informative piece of equipment and not just an appendage of the anæsthetic machine with the help of which he can on occasion hurry oxygen to a cyanosed patient.

SUMMARY

A study has been made of the expiratory phase of respiration in patients under general anæsthesia. Attention has been drawn to the fact that in certain circumstances the force of expiration varies with the depth of anæsthesia and can, in fact, be used to give a reliable measure of anæsthetic depth if certain basic principles are followed. An "Expiratory Pressure Test" has been described which enables the anæsthetist to take advantage of this interrelation and which facilitates the maintenance of anæsthesia at any desired level. Application of this principle in special cases has been more fully described, namely in general and supplementary cyclopropane anæsthesias, open anæsthetics, thoracic surgery, operative shock. It is thought that in the teaching of students attention should be drawn to the significance of expiratory signs since these signs may be clearly presented in cases where the classical signs of anæsthesia are poorly developed or obscured.

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In a survey by Gounelle, Vallette and Moine it is shown that compared with the pre-war sizes, the average height of boys and girls is less by 2 to 3 cm. whilst all pre-war statistics showed an increase of height.

The consequences of food shortage on height and weight increase have also been felt in the adolescent stage as is shown by the survey of Gounelle and Bachet, who in 1944 examined young men of 20 years who were supposed to go and work in Germany. Out of 125 of these boys 31 lost 16 lb. and over; 48 lost from 8 to 16 lb.; 17 lost 6 lb.; 29 had not lost weight.

Approximately one-third or one-quarter of all children and adolescents are in a poor state of health.

Digestive troubles have greatly varied. With babies gastro-enteritis owing to impure milk has been more frequent than before the war—this has been especially noticeable in Southern France and Marseilles. In older children troubles similar to those of adults have been noticed—dyspepsia due to too much roughage.

Psychological reactions in young children were very evident, such as tiredness without loss of intelligence, difficulty in attending, dreaminess, agitation with strong reactions almost convulsions, nightmares, fainting fits, throat spasms, muscular cramps, spinal pains. Reflexes are often exaggerated—Chvostek's sign is common—Erb's and Trousseau's signs are unusual. These signs can be related to spasmophilia and where it was possible to study these cases it has been found that calcium in the blood was insufficient—chronicaxics are increased and irregular—pH of urine is increased. All schoolmasters have noticed a lack of attention in their pupils and less efficiency, especially after air raids. Many cases of scoliosis were noted in children who had lost weight.

Infectious diseases.—Cases of diphtheria and typhoid have increased during these years. Lack of heating has caused an increase in colds, sore throats, bronchitis and bronchopneumonia, but no influenza epidemics have been noted. Conditions have become worse during this winter when the intense cold has caused capillary bronchitis, rapidly fatal in babies.

Such hard living conditions have naturally brought about an increase of the death-rate among children in France. Mortality has increased from 63 per thousand in 1939 to 91 per thousand in 1940 and 75 per thousand in 1943—12 per thousand more than in 1939.

As we have seen these death increases are not due to food shortage from 0 to 1 year of age. The high rate of 91 per thousand in 1940 was due to the exodus and resulting bad living conditions during the summer months—the following years the percentage remained high without reaching that maximum.

In the country these high death-rates may also be due to difficulties in getting a doctor in time—no motor car or no gasoline. Medicines or special food cannot be found in chemists' shops. In Paris, this has not been the case—medical care being regularly available. Lack of domestic heating in January 1945 has caused an increase in the death rate for babies 0 to 1 year of 40 per thousand compared with 1944.

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Skin diseases have greatly increased—acariasis in Paris has increased from 6,000 to 120,000 in 1943. Children have been affected, and, soap as well as medicine lacking, cases have been very difficult to cure and recur over and over again, owing to promiscuous living conditions and lack of transport.

The most serious problem is that of tuberculosis. All doctors have noticed the increase of serious tuberculosis cases. Figures are striking and we must point out that they are a low estimate—owing to the difficulties in statistics during the actual period. Tuberculosis is such an important factor for our children that I wish to quote a few figures showing the increased mortality from tuberculosis. If we compare 1943 with 1935 to 1938, there is an increase of 11%. In certain counties the increase is tremendous: 74% for the Bouches-du-Rhône (Marseilles); 69% for the Var (Toulon); 38% for Vaucluse. If we consider age and sex we find that for boys between 15 and 19 there is an increase of 25%; between 20 to 24 years an increase of 30.8%, and for girls 15 to 19, 23%; 20 to 24, 13%. In Paris the increase of new cases

of tuberculosis—comparing the years 1941 and 1942 with the years 1937 and 1938—shows an increase of 48%. Such was the situation in 1943. It has in no way changed in 1944. The first term of 1944 is the same as in 1943. First manifestations of tuberculosis are more severe and the number of fatal cases of tuberculosis from the beginning have increased.

The percentage of cases admitted at the Brevannes Sanatorium increased from 15% in 1937 and 8% in 1938 to 45% in 1941, and this figure has not changed since. This shows that almost half of the children cared for in a tuberculosis hospital have no chance of recovery. We must add to this an increase of 17% of cases of tuberculous meningitis. In all this it is obvious that malnutrition plays a large part.

Dealing with crime among youth, we have noted that doctors referred to various psychological troubles—lack of concentration and of stability among the children—this we have to bring in direct relation with an increase in youthful misdemeanours shown by the following figures: 1940, 16-937; 1941, 32-327; 1942, 34-781; 1943, 32-290.

French children were subjected to brutalities during the Occupation. Thousands were snatched from their parents during nightly police raids. Hundreds of young women gave birth to their children in prison and did not know what happened to them afterwards. During that terrible night of July 17, 1942, which all Parisians will remember, 3,000 Jewish children were separated brutally from their mothers and packed in the Velodrome d'Hiver where they lived for three days without food or care. I remember that several of my nurses gathered the pieces of bread left by their patients to take to them. We have no idea of what happened to these children. A great number were sent to Germany and died in the trains. Children of 8 or 10 years of age were packed with newborn babies. The ghastly story of Oradour is well known where the children of the village were brought into the church by German soldiers and then the church was set on fire with mothers and children in it.

Whole families, children included, were shot in many of our villages.

Other children were victims of the war itself: 200 children of Calvados county have had amputations but we lack orthopaedic apparatus for them.

Such was life for four years and as a result such was our children's welfare. We would like to say that things are better now—unfortunately it is not so. The milk supply for large towns and the Mediterranean districts has never been so bad.

The danger of tuberculosis appears to be even more serious for the months to come, when our prisoners will at last be coming back—the amount of tuberculosis among them being very high: 250,000 cases. There is a lack of adequate sanitary conditions and accommodation. There is also the psychological aspect of the problem: how can we prevent these men, separated from their families for five years, returning to them? Yet their return may give rise to many new cases among their children.

Another of our worries is due to the misery of devastated districts—the lack of medicines and coal, doctors unable to see their patients and we shudder at the idea of epidemics in such districts.

But we have hope for our race: Births are increasing—145 per 10,000 for 1938; 159 per 10,000 for 1943. France, like Great Britain, has felt the danger of reduced birth-rate and this increase, vital reaction of a people, is the best proof of its future greatness.

I must add that youths have been taking part in Resistance—have been used as liaison officers—have helped our secret service—have taken arms to avenge their fathers or brothers. Many heroic children are among our Resistants and F.F.I. and the sacrifice of these martyrs is also a certainty of our greatness.

Child Life and Health in Belgium during and after the German Occupation. [Abstract]

By R. W. B. ELLIS, O.B.E., M.D.,

Wing Commander, R.A.F.V.R.

THE German occupation of Brussels lasted from May 1940 to September 1944. From a retrospective survey in the winter of 1944-45, an attempt has been made to determine the effect of the Occupation on the children of Belgium, information being based on numerous interviews with children, parents, doctors and school teachers, and visits to infant welfare centres, crèches, orphanages, school medical examinations, and hospital clinics. From the psychological aspect, the opinion was formed that the effect on the children had been much less than on their parents. There had been the inevitable results of broken homes due to death, political imprisonment or other causes; evacuation to foster-parents or children's colonies; and closure of schools for varying periods owing to bombardments or lack of coal. The suspicion of "informers" had in some cases

The National Department of Statistics published the results of the school medical examinations for the Southern area—12,696 boys and 12,648 girls. This survey showed a decrease in weight of 2 to 14 lb. for the boys (according to age) as compared with the average weight of 1938—the situation is similar for the girls.

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of tuberculosis—comparing the years 1941 and 1942 with the years 1937 and 1938—shows an increase of 48%. Such was the situation in 1943. It has in no way changed in 1944. The first term of 1944 is the same as in 1943. First manifestations of tuberculosis are more severe and the number of fatal cases of tuberculosis from the beginning have increased.

The percentage of cases admitted at the Brévannes Sanatorium increased from 15% in 1937 and 8% in 1938 to 45% in 1941, and this figure has not changed since. This shows that almost half of the children cared for in a tuberculosis hospital have no chance of recovery. We must add to this an increase of 17% of cases of tuberculous meningitis. In all this it is obvious that malnutrition plays a large part.

Dealing with crime among youth, we have noted that doctors referred to various psychological troubles—lack of concentration and of stability among the children—this we have to bring in direct relation with an increase in youthful misdemeanours shown by the following figures: 1940, 16-937; 1941, 32-327; 1942, 34-781; 1943, 32-290.

French children were subjected to brutalities during the Occupation. Thousands were snatched from their parents during nightly police raids. Hundreds of young women gave birth to their children in prison and did not know what happened to them afterwards. During that terrible night of July 17, 1942, which all Parisians will remember, 3,000 Jewish children were separated brutally from their mothers and packed in the Velodrome d'Hiver where they lived for three days without food or care. I remember that several of my nurses gathered the pieces of bread left by their patients to take to them. We have no idea of what happened to these children. A great number were sent to Germany and died in the trains. Children of 8 or 10 years of age were packed with newborn babies. The ghastly story of Oradour is well known where the children of the village were brought into the church by German soldiers and then the church was set on fire with mothers and children in it.

Whole families, children included, were shot in many of our villages. Other children were victims of the war itself: 200 children of Calvados county have had amputations but we lack orthopaedic apparatus for them.

Such was life for four years and as a result such was our children's welfare. We would like to say that things are better now—unfortunately it is not so. The milk supply for large towns and the Mediterranean districts has never been so bad.

The danger of tuberculosis appears to be even more serious for the months to come, when our prisoners will at last be coming back—the amount of tuberculosis among them being very high: 250,000 cases. There is a lack of adequate sanitary conditions and accommodation. There is also the psychological aspect of the problem: how can we prevent these men, separated from their families for five years, returning to them? Yet their return may give rise to many new cases among their children.

Another of our worries is due to the misery of devastated districts—the lack of medicines and coal, doctors unable to see their patients and we shudder at the idea of epidemics in such districts.

But we have hope for our race: Births are increasing—145 per 10,000 for 1938: 159 per 10,000 for 1943. France, like Great Britain, has felt the danger of reduced birth-rate and this increase, vital reaction of a people, is the best proof of its future greatness.

I must add that youths have been taking part in Resistance—have been used as liaison officers—have helped our secret service—have taken arms to avenge their fathers or brothers. Many heroic children are among our Resistants and F.F.I. and the sacrifice of these martyrs is also a certainty of our greatness.

Child Life and Health in Belgium during and after the German Occupation. [Abstract]

By R. W. B. ELLIS, O.B.E., M.D.,
Wing Commander, R.A.F.V.R.

THE German occupation of Brussels lasted from May 1940 to September 1944. From a retrospective survey in the winter of 1944-45, an attempt has been made to determine the effect of the Occupation on the children of Belgium, information being based on numerous interviews with children, parents, doctors and school teachers, and visits to infant welfare centres, crèches, orphanages, school medical examinations, and hospital clinics. From the psychological aspect, the opinion was formed that the effect on the children had been much less than on their parents. There had been the inevitable results of broken homes due to death, political imprisonment or other causes; evacuation to foster-parents or children's colonies; and closure of schools for varying periods owing to bombardments or lack of coal. The suspicion of "informers" had in some cases

The National Department of Statistics published the results of the school medical examinations for the Southern area—12,696 boys and 12,648 girls. This survey showed a decrease in weight of 2 to 14 lb. for the boys (according to age) as compared with the average weight of 1938—the situation is similar for the girls.

In a survey by Gounelle, Vallette and Moine it is shown that compared with the pre-war sizes, the average height of boys and girls is less by 2 to 3 cm. whilst all pre-war statistics showed an increase of height.

The consequences of food shortage on height and weight increase have also been felt in the adolescent stage as is shown by the survey of Gounelle and Bachel, who in 1944 examined young men of 20 years who were supposed to go and work in Germany. Out of 125 of these boys 31 lost 16 lb. and over; 48 lost from 8 to 16 lb.; 17 lost 6 lb.; 29 had not lost weight.

Approximately one-third or one-quarter of all children and adolescents are in a poor state of health.

Digestive troubles have greatly varied. With babies gastro-enteritis owing to impure milk has been more frequent than before the war—this has been especially noticeable in Southern France and Marseilles. In older children troubles similar to those of adults have been noticed—dyspepsia due to too much roughage.

Psychological reactions in young children were very evident, such as tiredness without loss of intelligence, difficulty in attending, dreaminess, agitation with strong reactions almost convulsions, nightmares, fainting fits, throat spasms, muscular cramps, spinal pains. Reflexes are often exaggerated—Chvostek's sign is common—Erb's and Trousseau's signs are unusual. These signs can be related to spasmophilia and where it was possible to study these cases it has been found that calcium in the blood was insufficient—chronaxies are increased and irregular—pH of urine is increased. All schoolmasters have noticed a lack of attention in their pupils and less efficiency, especially after air raids. Many cases of scoliosis were noted in children who had lost weight.

Infectious diseases.—Cases of diphtheria and typhoid have increased during these years. Lack of heating has caused an epidemic in colds, sore throats, bronchitis and bronchopneumonia, but no influenza epidemics have been noted. Conditions have become worse during this winter when the intense cold has caused capillary bronchitis, rapidly fatal in babies.

Such hard living conditions have naturally brought about an increase of the death-rate among children in France. Mortality has increased from 63 per thousand in 1939 to 91 per thousand in 1940 and 75 per thousand in 1943—12 per thousand more than in 1939.

As we have seen these death increases are not due to food shortage from 0 to 1 year of age. The high rate of 91 per thousand in 1940 was due to the exodus and resulting bad living conditions during the summer months—the following years the percentage remained high without reaching that maximum.

In the country these high death-rates may also be due to difficulties in getting a doctor in time—no motor car or no gasoline. Medicines or special food cannot be found in chemists' shops. In Paris, this has not been the case—medical care being regularly available. Lack of domestic heating in January 1945 has caused an increase in the death rate for babies 0 to 1 year of 40 per thousand compared with 1944.

There have been no considerable ailments due to lack of vitamins, as might have been feared, thanks to the good old French food customs.

These are the great troubles caused by food shortage—but there are many others: amenorrhœa in young girls; chilblains, a painful ailment for children and adults. Many authors have sought a biochemical explanation but we believe cold, especially in houses, to be the main cause.

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Section of Odontology

President—H. T. ROPER-HALL, M.B., M.D.S.

[February 26, 1945]

Cysts Involving the Ramus of the Mandible

By D. GREER WALKER, M.Dent.Sc., M.B.

DURING the past three years a number of cases of odontomes have been admitted to Stoke Mandeville Hospital. The greater proportion of these have been dental and dentigerous cysts. It has long been recognized that the treatment of these cysts presents little difficulty and the simplest operative procedures suffice to attain the desired result. In contrast, the rarer type, the adamantinomatous cyst, is always a problem demanding a more radical treatment to prevent recurrence. This difference in behaviour of these cysts has led to the conclusion that the recurrence of any cyst in the jaw following operation is indicative of an adamantinoma.

In our series, Professor Kilner and I have found three cases presenting the history of repeated operations in spite of the fact that radiological examination did not suggest an adamantinomatous nature. In each case the cysts occurred in the ramus of the mandible; in two of them both rami were involved by separate cysts, suggesting a cystic diathesis. Two cases were dental cysts, and the third, dentigerous with bilateral cysts.

This rather odd clinical observation, the recurrence of simple cysts, prompted Professor Kilner and myself to attempt to find an adequate explanation. Doctors Scarff and Murray reported in all three cases following an operation histological findings typical of dental and dentigerous cysts. We therefore felt that two factors might well be responsible for the recurrence of the cysts: (a) Incomplete removal of all cyst lining when the condyloid and coronoid processes are involved. (b) The stenosis of the orifice of the cyst leading to obliteration. The extensive raw area left after the wide reflection of the tissues is bound to cause scarring with the accompanying contraction.

We feel that these two factors may well account for the recurrence, and in view of this we have adopted the following procedure at operation:

An incision is made from the molar region extending up the anterior border of the ramus. The tissues are widely reflected and the cyst cavity opened; after adequate removal of bone, this opening is enlarged and the cyst lining removed. When dealing with a dentigerous cyst the offending tooth is extracted. The bone edges are trimmed and the final stage consists of inserting a stent mould carrying a Thiersch graft to cover the raw margins of the orifice. Adequate stabilization of the mould is achieved by a couple of silk sutures inserted in the surrounding margins. On removal of the mould the subsequent treatment consists of replacement by a "plug" attached to a denture.

A fourth case, one of Mr. Elliott Blake's, a dentigerous cyst occurring in a boy aged 14, with the third molar lying high in the ramus, was treated in a similar manner. No operations had been performed previously in this case.

Our results so far have been gratifying, and the cavity has remained saucerized showing no signs of stenosis of the orifice.

Professor Kilner and I would hesitate to say that this skin-grafting operation is essential, but we are of the opinion that it greatly simplifies the treatment of these cases. It is hoped that we shall be in a position to report on the further progress of these cases when we review our epithelial odontomes at a later date in conjunction with our pathological colleagues.

We should like to thank Professor McIntosh, Director of the Pathological Department, and Doctors R. W. Scarff and John Murray for their help on the histology. We are indebted to Dr. C. W. C. Gough for his radiographs; and to the Director General of Medical Services of the Ministry of Pensions for permission to publish this paper.

entered into school life, and certain activities such as scouting had been officially curtailed. In some of the poorer schools, intellectual apathy due to deficient diet or cold had been apparent. But in general the disturbance of normal routine did not appear to have left any serious permanent effects.

With regard to nutrition, a policy had been adopted from the start of safeguarding the younger children at the expense of older children and adults. Thus during the period of severest deprivation (1941-42), the official rations for children under 3 were more than sufficient and those for children up to 6 were adequate; adolescents from 14 to 18 were allowed approximately half their normal caloric requirements, whilst over 18 the official rations provided only 1,230 calories a day. Even this amount was very seldom actually received on the ration by the older age-groups, whereas the youngest children's rations, which included milk, were usually obtainable or even supplemented in cases of debility or illness. Survival was only possible at this time by organization of the miscalled "Black Market", a crude but effective system by which members of nearly every urban family would make frequent visits to the surrounding country to buy and carry home farm produce (which would otherwise have been requisitioned by the invader) and reselling or exchanging what was not required for home consumption. Many urban children were billeted with peasant families, received in children's colonies under the Œuvre Nationale de l'Enfance, or they had supplementary meals in open-air schools or holiday camps through the Secours d'Hiver.

The chief deficiencies in the diet, apart from total calories, were fat and first-class protein; but in 1941-42 the bread was so bad that it was described as being like soft putty and was often uneatable. Older children (who received no milk) also suffered a serious deprivation of calcium, though younger children received calcium and vitamin supplements distributed through welfare centres and schools.

There do not appear to have been any large-scale epidemics amongst children during the war years. There was an increased incidence of scabies, impetigo, and osteomyelitis secondary to skin-sepsis (due to lack of soap and fuel), and probably an increase in juvenile tuberculosis in 1942, though the war figures for this are unreliable. Judging by hospital admissions, there was no increase in infantile scurvy and little or no childhood pellagra. Famine œdema in childhood was extremely rare, though several hundred cases were observed in adults, mostly over 40, in one clinic. The incidence of rickets is difficult to estimate; it is certainly common in Belgium to-day and has probably increased during the war, but examinations of older children suggest that the incidence was also high pre-war. Enuresis, possibly dietetic in origin, became extremely frequent during the war years.

Dr. Ellis presented a detailed study of a working-class family with three children aged 13, 11, and 3, in order to illustrate the *modus vivendi* during the war and the ultimate result. Clinical and radiological examination of the children showed them to be healthy and of normal development for age, with the exception of genu valgum in the youngest and slight rachitic deformities of the thorax in the two elder children. The weekly budget in February 1945 showed that the whole of the week's wages (249 fr.) was expended on rent, light, fuel and soap, whilst the 399 fr. spent on food was met by manipulation of the Black Market or from savings.

Height and weight statistics prepared from groups of 60 school children aged 7 to 8, 9 to 10, 11 to 12, and 13 to 14, from a working-class urban commune, for each of the war years, showed that the average height and weight of each group of the same age were lower in 1944 than in 1939 or 1940, but that the curves suggested prolonged subnutrition rather than acute malnutrition in any one year.

Onset of puberty.—Examination of 40 boys aged 13 to 17 in two orphanages showed no significant delay in the onset of puberty, but extra rations had been received in both institutions. A group of 64 "normal" schoolgirls aged 15 to 17 living at home in a working-class district showed complete or prolonged amenorrhœa in 17%; irregular and scanty menstruation in a further 20%; and the occurrence of the first period after the age of 15 in 52% of those who had menstruated. These findings were regarded as definitely indicating a delay in the average age of establishment of puberty.

In conclusion, it was emphasized that whilst little evidence of permanent retardation of growth or ill-health was seen amongst the younger children at the present time, those likely to have suffered most were the adolescents and young adults who were aged 12 to 16 years in 1941-42. This was reflected in the number of recruits at present failing to reach pre-war Belgian Air Force standards. All children had suffered severely during the bitter weather in January 1945 owing to the lack of fuel and clothing. The food situation up to that time had shown little improvement since the Liberation (and in fact milk had been in shorter supply than ever before), but at the time of writing there were signs that conditions were improving.

In three cases sterile abscesses have occurred in the first week. These were probably due to the breakdown of overlying soft tissue involved in the original inflammatory reaction and, after the necessary evacuation, healing occurred in two or three days.

In three other cases apparently similar abscesses showed the persistent presence of organisms and here the indications are very different. The persistence of an infective discharge is an indication that the original surgery has been insufficiently radical and the patient must therefore be returned to the operating room for completion of his excision.



FIG. 2(a)



FIG. 2(b)



FIG. 2(c)

FIG. 1.—Diagrammatic illustration of the amount of excision necessary to eliminate all infected bone. The saucerization of the ends to enable the soft tissues of the cheek to obliterate the cavity and the position of the penicillin tubes is clearly shown.

FIGS. 2(a), (b) and (c) (above).—2(a) Pre-operative swelling in the case of osteomyelitis localized in the region of the right angle. (b) The wound one week after operation with the penicillin tubes in place. (c) Post-operative result.

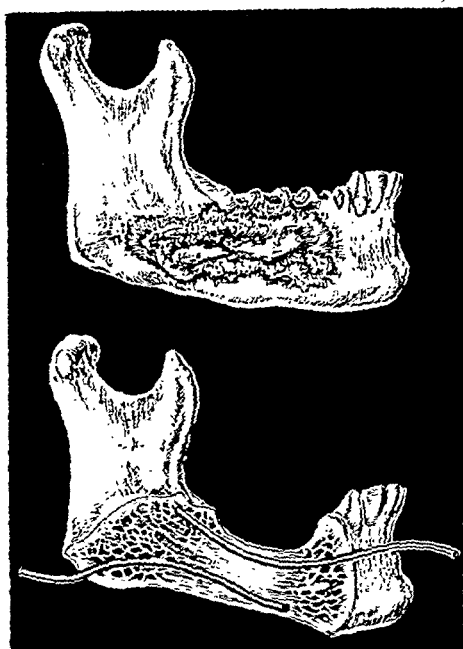


FIG. 1

It is unnecessary and undesirable to delay this in the hope that the condition will clear spontaneously as it has been found that the second operation revealed a clearly defined area of dead bone which had been overlooked.

The whole principle of surgical closure depends for its success upon the obliteration of all cavities and when this cannot be achieved skin closure is unwise. When the infection is confined to the lingual aspect of the body of the mandible, access can be gained only by stripping the muscles of the floor of the mouth from the jaw. I have never succeeded in bringing them back and maintaining them in close apposition with the excised area

Osteomyelitis of the Jaw

By RAINSFORD MOWLEM, F.R.C.S.

ON rare occasions osteomyelitis of the mandible may be caused by organisms reaching the bone via the blood-stream or by direct extension from an adjacent infected focus. but in most cases it is due to invasion by organisms commonly found in and entering from the mouth. They gain access through a tooth socket, through a fracture line, and sometimes through an apparently intact mucosa, so that every extraction or even a minor lesion such as gingival incision, or a pressure ulcer, may provide a potential site of entry for infection. At the same time the hazard of bacterial invasion occurs many thousands of times for every one occasion upon which gross infection results, and as there does not appear to be any specific bacterial cause there must be some other determining factor. This, in my opinion, is related to the normality of blood supply. When bone involvement does supervene, then here as elsewhere the disaster is primarily vascular. So long as the extremely generous network of vessels remains intact, trauma is rapidly followed by the erection of a leucocytic barrier which deals with such organisms as are present. Damage to the vascular supply precludes this reaction and the degree of damage will determine the amount of bone infection.

Every extraction crushes a thin lamina of bone and its contained vessels will clot. In the normal course of events a layer of granulation tissue will cover and resorb the exposed bone. If the damage is a little more extensive, thrombosis extends further back and the protective barrier becomes sufficiently remote to exclude pieces of bone large enough to be visible to the naked eye. If the process goes further still and is no longer confined to the small vessels around the socket but involves the inferior dental vessels, then the barrier to invasion is so remote that a large area of the jaw is dead and is therefore the ideal site for organismal invasion. In support of this theory is the fact that in the present series of 45 cases, only one of those which have followed tooth extraction has been related to a tooth further forward than the second premolar. In other words, removal of those teeth which may result in thrombosis of a large subjacent vascular bundle in the inferior dental canal is more prone to be followed by infection than is the removal of anterior teeth which have no such vascular relationship.

Now we have the acute disaster of osteomyelitis. The patient suffers immediate and considerable pain. Extensive swelling of the cheek and soft tissues of the mouth soon follows and is associated with systemic disturbance. In many instances an immediate and persistent mental anaesthesia is present. The end-result of the condition and the time at which it is reached will depend largely on the treatment we employ. We can apply heat to encourage an improvement in blood supply so that in the course of time the dead and infected bone will be thrown off either microscopically in the form of pus or macroscopically as sequestra. Abscesses are drained as they occur, sequestra removed as they separate, and devitalized teeth extracted as they are noted.

In the course of time the process will be completed and the patient will have recovered. If the initial involvement be small he may be fit in a comparatively few weeks but if it be extensive the period may lengthen to months and years and the final result will never approximate to dental or cosmetic perfection.

The other course of treatment depends upon one's opinion as to the underlying pathology. If vascular insufficiency is the important factor it seems unreasonable to leave a mass of dead bone in direct communication with the infected mouth. This tissue has no power of resistance to infection and its behaviour is a foregone conclusion. I prefer, therefore, to remove these areas as soon as their extent can be determined. Obviously the central area of the mandible is the only one at first concerned but it is bad surgery to clear out the centre of the bone leaving a cortical shell surrounding the cavity. The lower margin of the jaw—which is dense cortical bone possessing a poor blood supply and therefore a poor resistance to infection—is first removed and then the outer plate is cut away to expose the affected area. Excision is continued until nothing but bleeding healthy bone is left (fig. 1). The defect as a whole is saucerized so that after any mucosal defects have been closed the soft tissues of the cheek collapse into and obliterate the resultant cavity. These soft tissues are a source of further blood supply which helps to eliminate such infection as has been spread during the surgical intervention. Two to four thousand units of penicillin per day are used as a local adjuvant to this process of sterilization and are continued for from seven to ten days (fig. 2). Care must be taken to avoid the introduction of non-sensitive organisms such as *B. coli*, *B. proteus* or *Ps. pyocyanea*.

At the end of a week the external wound and any mucosal openings have healed, the process of infection has ceased and the phase of bone regeneration has commenced. This of course is the optimal behaviour but we have encountered divergencies from it, some of which, however, are controllable.

In the present series of cases only three have been sent for treatment within less than five weeks from their earliest symptoms whilst the longest recorded time was over seven hundred and fifty weeks. Even if we exclude the seven cases of over one hundred weeks' duration we still have an average of ten weeks between the onset of symptoms and the institution of radical surgery. It should be possible to decide that surgery is indicated earlier than this and thereby minimize both the magnitude of the operation and the discomfort of the patient.

I am glad to acknowledge the invaluable assistance of my dental and surgical colleagues of the Plastic and Jaw Centre at Hill End Hospital, and I am also indebted to members of the records section for the illustrations used in this paper.

Mr. Nils L. Eckhoff: I am personally indebted to Mr. Mowlem for bringing to my notice a year or two ago the great value of the radical attack in osteomyelitis of the jaw when the acute stage is passed. Like many surgeons I had been inclined to treat this disease conservatively, by incision and sequestrectomy as occasion demanded. The conservative outlook is no doubt an outcome of the more conservative treatment of osteomyelitis of the long bones. During the last twenty years surgeons have given up the guttering operation, so common in our youth, for removal of a small piece of cortex, with a few drill holes in addition, vaseline gauze pack, and immobilization in plaster of Paris. This method has been used extensively in war surgery, and is known by the name of Winnett-Orr. In certain special cases recovery has followed immobilization in plaster without surgical incision, and penicillin may further modify the picture.

It might therefore appear that radical surgery in jaw osteomyelitis was a retrograde step. But we must at once realize that mandibular osteomyelitis is very different from the disease in the long bones. The latter is essentially a septicæmia from the start, and may involve a second or third bone, if not at the same time, then very soon afterwards. It also produces secondary abscesses in the lung, heart, kidney and other tissues. The offending organism is usually the *Staphylococcus aureus*. In the jaw the disease is very rarely blood-borne. It may be so in children, during acute fevers, but I believe that such infections are most probably due to acute middle-ear disease, the infection spreading to the jaw through the incompletely ossified temporal bone. In most other cases the infection is conducted to the jaw, from the mouth, via the teeth. The organism is usually a hæmolytic streptococcus, or a mixed infection.

In the long bone pus is pent up in the medulla, and can only escape with great difficulty through the relatively thick cortex. In the jaw pus can readily escape into the mouth, or through the relatively thin cortex into the submandibular tissues. This must explain why jaw osteomyelitis is (happily) uncommon, whereas alveolar abscess is so common. My dental colleagues at Guy's tell me that there are probably 500 cases of alveolar abscess per annum, but only two or three cases of osteomyelitis in the same time.

I have for some time attempted to find a detailed description of the blood supply of the jaw. Hankey attempted to work it out by studying the shape and size of sequestra. But I feel sure that in most cases sequestration is of relatively small order, due to thrombosis of the smaller arteries, and the main inferior dental is not frequently responsible. Minor cases respond well to simple incision and sequestrectomy, and I know of a few that have not even required this. I feel it would be dangerous if surgeons up and down the land performed the radical operation in every case diagnosed. Selection of cases is of extreme importance.

Similarly the time of attack has to be carefully chosen. Just as surgeons learnt the danger of radical surgery in the long bones, so also must we learn the danger of radical surgery in jaw osteomyelitis in the acute stages. Miltner and Wolfe pointed this out in 1934.

The exact relationship between alveolar abscess and osteomyelitis is not quite clear. Some dental surgeons would always extract a tooth in the presence of an abscess, others would certainly not do so. The possible legal complications should osteomyelitis follow extraction are well known. Suffice it to say that most cases that I have seen have presented themselves with a history of pain and swelling, extraction, further pain and swelling, further extraction, &c. I would plead for the most careful consideration of the indications for extraction, and the even more careful execution of such extraction in the presence of inflammation.

From the analogy of the beneficial effects of immobilization in limb osteomyelitis, I feel there is a definite place for immobilization in jaw osteomyelitis, quite apart from the danger of pathological fracture. I have used it with satisfaction in several cases, and would always advise it in the acute stages.

There are varying degrees of osteomyelitis, and all cases do not behave alike. I would suggest that radical surgery should never be employed in the first three weeks, owing to the danger of fulminating septicæmia and death. But if after cautious extraction, preferably not repeated, drainage of abscesses and immobilization, symptoms of pain, swelling and discharge continue for three or more weeks, it is then clearly indicated. We should also discuss the relationship between alveolar abscess and osteomyelitis, the value of limited attack in certain cases, the value of immobilization, and the desirability of combined intra-oral and extra-oral attack, in those cases requiring radical surgery.

We have seen the excellent results of radical surgery combined with penicillin. I should like to point out that it is the radical surgery that is important, *lest surgeons are inclined to spare the knife for the drug*. Penicillin can never rid the patient of dead bone, nor will it reach such bone, for it has no blood supply.

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and I think that in these circumstances it is better to revert to the older method of packing the cavity to ensure slow granulation from its base. This is a tedious process but is preferable to the repeated breakdown after partial healing which will otherwise occur.

Another complication may be encountered in extensive lesions. Removal of all infected bone will either reduce the mandible to an extremely narrow bridge or will sever it completely. In five instances it has been found preferable to continue with the eradication of all diseased bone in spite of the creation of a fracture. If one fails to eliminate the infection a spontaneous break will occur in the presence of diseased bone and the healing process, if it occurs at all, will be slow. On the other hand if infection is radically dealt with union occurs rapidly, even though fixation of the fragments is impracticable (fig. 3). In any case it seems preferable to concentrate upon the elimination

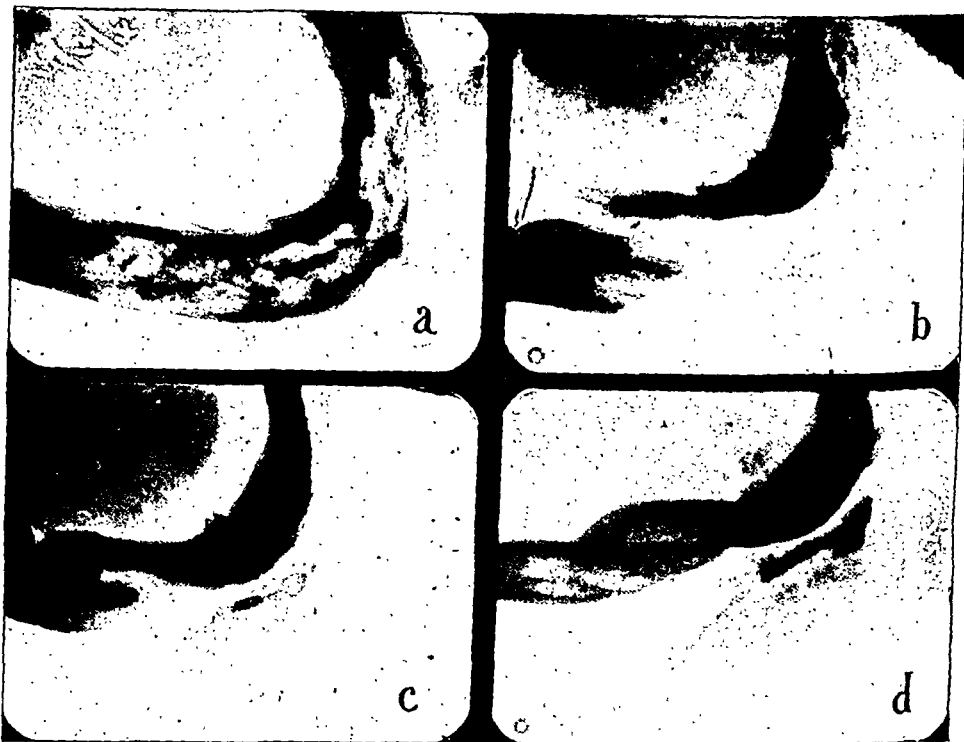


FIG. 3.—Occlusal views of the body of the mandible. (a) Shows extensive osteomyelitis (b) Shows complete division of the jaw whilst (c) and (d) illustrate regeneration of the bone.

of infection, for even if this should be followed by non-union the subsequent bone graft can be applied in the matter of a few weeks.

Now it is clear that the treatment just described and some of its complications are by no means minor matters. An external approach with skin scarring is inevitable but even initially this scar should not be excessive and in any case it is capable of later improvement. It in no way compares with the soft tissue damage caused by long-continued bone infection.

We are all familiar with the relatively acute "flare up" after an extraction which soon settles down and it is necessary to distinguish between this and the true osteomyelitis which will progress to still further bone destruction. In the early days X-rays are of no value as bone changes do not become evident for some weeks. Even later the radiographs may be misleading and will generally tend to cause an underestimation of the amount of real damage. It may be that anaesthesia over the distribution of the mental nerve occurring immediately, and persisting, is of importance as indicating damage within the inferior dental canal. There is, however, no real guide except the clinical condition and behaviour of the patient. The degree and persistence of swelling, pain, trismus and temperature, together with the amount and site of purulent discharges, are all indications of underlying bone involvement and should not be allowed to persist without the serious consideration of radical surgery.

two age-periods and blotted out many anatomical points (fig. 1). These tracings bring out some very important points about the development of the face from birth to adult: In the upper jaw—(a) The posterior end of the hard palate remains in almost the same vertical plane; (b) the alveolar ridge and the teeth travel downwards and forwards. It seems these facts can only be explained on the hypothesis that increase takes place by building up on the anterior and outer surfaces, in the alveoli and on the alveolar margins, which latter process carries the teeth downwards and forwards. In the lower jaw relative to the Bolton plane and the registration point: (a) The anterior border of the ascending ramus at its junction with the horizontal ramus remains in almost the same vertical plane; (b) the ascending ramus doubles in width from front to back between birth and adult; (c) the condyle travels back, by a reformation of the base of the skull a distance equal to the increase in width of the ascending ramus.

Thus room is obtained for the eruption of the successive molars by forward movement of the teeth anterior to them due to deposition in the alveoli. There is, in addition, upward and outward movement of the mandibular teeth through deposition, both alveolar and on the outer surfaces. This is, of course, counter to the view of Hunter [13] that room was made for the molars by absorption of the anterior border of the ascending ramus, compensated by deposition on the posterior border. Broadbent's tracings indicate that the major part of forward movement takes place after the eruption of the teeth. Tracings of the upper arch at different periods show the gradual migration forward of the deciduous teeth in relation to the posterior border of the hard palate and the erupting first and second permanent molars drop successively into the spaces thus obtained.

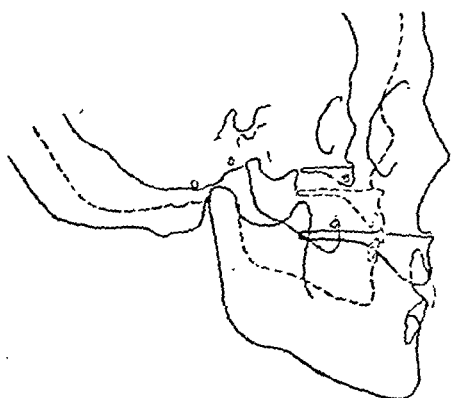


FIG. 1.

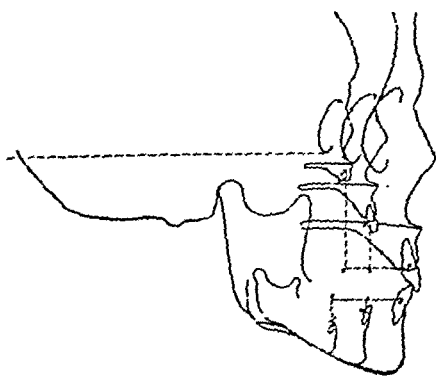


FIG. 2.

From these records of Broadbent we can also get a comparison of the relative amounts of forward and downward translations of the teeth in the upper, and of forward and upward translations in the lower (fig. 2). Birth, 3 years and adult tracings are superimposed again, but a perpendicular has been dropped from the mid-point of the birth alveolar crest to a line through the adult alveolar crest mid-point parallel to the Frankfurt plane. Also the birth mandible is superimposed with its lower border aligned on the lower border of the adult mandible and the anterior border of its ascending ramus in the vertical plane of the corresponding adult surface, and the same lines have been drawn as in the upper. The justification for this superposition of the lower border of the birth mandible on that of the adult is Brash's [3] demonstration that growth in height of the mandible is by addition to the upper and not to the lower border.

While the amount of upper and lower forward movements is nearly the same, the lower being slightly greater than the upper, in vertical change there is a very marked difference. That difference is clearly an important factor in the different behaviour of upper and lower molars when abnormal conditions permit migration. The vertical movement in the upper is very much greater than in the lower. The superposition demonstrates also the growth of the condyle [7] and ascending ramus which compensates in part for the downward growth of the upper and upward growth of the lower alveolar borders. The remainder of the compensation comes from the growth of the skull base carrying downward and backward the glenoid fossae.

[March 26, 1945]

Four Months in Tristan da Cunha. [Summary]

By Captain R. F. SOGNAES, M.S., Ph.D.

THE dental survey of Tristan da Cunha was carried out as part of the programme of the Norwegian Scientific Expedition to that island, December 1937 to March 1938.

The following findings were of particular dental interest:

- (1) A condition was seen suggestive of threshold dental fluorosis and a relatively high fluorine content of the teeth, apparently not water-borne alone.
- (2) The freedom from caries, particularly of those teeth developed early in life such as the deciduous dentition on the whole, and the six-year molars and anterior teeth of the permanent dentition.
- (3) The chronic type of caries and its low incidence, as well as very low and scattered counts of salivary *L. acidophilus* in all except a few physically defective males and the great majority of the older women, a situation that apparently cannot be explained by food habits alone.
- (4) The diet was monotonous diet (fish and potatoes); milk consumption and import of flour and sugar were less than was believed; in former days there was more per islander of every item of island food, as well as of food imported from whale boats.

Migrations of Teeth Following Extractions

By SHELDON FRIEL, B.A., M.Dent.Sc., Sc.D.

EARLY dental literature noted that there were changes in relationship of the teeth following extraction of deciduous or permanent teeth in the growing child. Hunter [14], Salzmann [15], Dewey [8] and other writers state that molars tend to come forwards, especially in the upper jaw and that teeth anterior to molars tend to go backwards, especially the lower second premolar after the loss of deciduous or first permanent molars. Turner [17] asserts that lower molars never move forwards.

It is now possible to fit these partial observations into a broader picture of facial development and tooth movement and when that is done it seems to me to call for a restatement of the limited phenomena seen by these observers. The general hypothesis which I have to present is that *all teeth move forwards and none backwards*. A break in the continuity of the arch made by tooth extraction may have different effects on the crowns and roots of teeth in different parts of the dentition, all of which can be explained in terms of the paths of eruption and of the forces acting on the teeth during eruption. These effects will be modified by the time of extraction, the tooth or teeth extracted, and by the normal or deficient growth of the individual.

There have been two outstanding advances in our knowledge of the manner of growth of the face and jaws and the development of the dentition since the work of Hunter [13]. The first, Brash's [1, 2, 3] madder-feeding experiments on the growth of the jaws in the pig, and the second, Broadbent's [4, 5, 6] serial X-ray examination of facial development. The conclusions of these two investigations are not opposed to one another but are complementary and have considerably modified our conception of the development of the dentition.

Broadbent took profile and full-face serial radiographs of children. From these radiographs he made tracings, which he then superimposed on each other. Each tracing was orientated by a registration point and a defined plane, the Bolton plane. This plane is formed by a line joining the nasion to the highest point in the profile of the notches at the posterior ends of the condyles of the occipital bone. The registration point is found by dropping a perpendicular from the centre of the sella turcica to the Bolton plane and bisecting this perpendicular; the point of bisection being the registration point. The registration point is in the body of the sphenoid bone, which is the area of greatest stability. The advantages of using the Bolton plane are its stability, and the fact that it separates the cranium from the face. Broadbent illustrates normal growth from birth to adult by a composite picture showing five age-periods. It is a difficult picture to analyse and consequently I have eliminated

(3) If unworn $\overline{76}$ are removed from a skull (fig. 4, p. 460), $\frac{6}{6}$ then occluded to their normal relationship for 7 years of age and $\frac{7}{7}$ in their normal relationship, it will be found that when $\overline{76}$ are in contact there is always a space between $\overline{76}$ showing that $\overline{6}$ must alter its relationship with $\overline{6}$ and move forward. This occurs after the loss of $\frac{e\ d\ c}{e\ d\ c}$ (fig. 5). The medio-buccal cusp point of $\overline{6}$ is no longer anterior to the buccal groove of $\overline{6}$ but opposite it. The cusp point of $\overline{7}$ can then be opposite the buccal groove of $\overline{7}$. In $\frac{7}{7}$ the triangular ridges of the medio-buccal cusps run more transversely than in $\frac{6}{6}$ so that the point of the cusp and triangular ridge are more in line. It is sometimes stated that the greater forward movement of the lower deciduous teeth as compared with the upper between 3 and 7 years of age is not necessary as after the loss of $\frac{e\ d\ c}{e\ d\ c}$ $\overline{6}$ will move forward more than $\overline{6}$ and will allow $\frac{6}{6}$ to occlude, the triangular ridge of the medio-buccal cusp of $\overline{6}$ being in the buccal groove of $\overline{6}$. I have not yet seen a case where these two types of forward movement described under headings (2) and (3) are not necessary for the ideal occlusion of the second molars [10].

(4) It sometimes occurs that $e\ d$ are lost some time previous to $\overline{e\ d}$ and vice versa [10]. In serial models of these cases the forward movement of $\overline{6}$ or $\overline{6}$ following alternate loss of e or e can be demonstrated.

The evidence that I have put before you of the normal development of the jaws and the dentition is altogether in favour of the forward movement of all teeth and I have not been able to find any evidence that teeth move backwards except when driven backwards by an outside force, e.g. an erupting canine might drive a first premolar distally where there was room for the tooth to move.

What I have described is the normal course of events during development. But with the loss of a unit or units from the dentition before the eruption of the "replacement" teeth is complete, we get, as Hunter and others said, considerable changes in the subsequent picture. The changes vary in degree with the time at which the unit is removed and with the vigour of growth of the jaws, but the general tendency is for the forward movement of the roots to continue whilst the crowns of the teeth other than the molars lag behind. This tendency is most pronounced in the lower second premolar but it exists in all teeth other than the molars. One sees at times even the centre point of the upper or lower arch shifting towards the side from which a tooth, even as far back as a first permanent molar, has been lost, due to the lag of the anterior segment on the side of the extraction. Obviously the explanation lies in the loss of continuity of the arch. The pressure of crown on crown is clearly an important factor in keeping teeth vertical while their roots are carried forward. What requires elucidation is mainly the difference in degree of distal tilt assumed by upper and lower premolars in general and the extreme case of the lower second premolar.

My thesis is that my diagram supplies a large part of the answer. $\overline{7}$ has normally about four times as far to travel as $\overline{7}$ in vertical movement to get into place behind $\overline{6}$. To get into the place of $\overline{6}$ when that tooth is lost a slight change of angle of descent, and hence only a slight increase in distance of movement, is necessary. $\overline{7}$ in similar circumstances has to make a much greater change of angle and consequently the increase of travel called for is much greater. We can reduce that statement to figures with fair accuracy (fig. 6). Assuming at the time of extraction of $\overline{6}$, $\overline{7}$ has still 6 mm. of vertical movement to get into its normal occlusion (which is probably a reasonable figure, but any other figure can be assumed without affecting the argument) then $\overline{7}$ will have 24 mm. to travel. Now suppose $\overline{6}$ removed. If $\overline{7}$ is to get into a position where it will replace $\overline{6}$ the shortest distance it can travel will be (taking the medio-distal diameter of $\overline{6}$ as 12 mm.) a fraction over 13 mm. or rather more than double its normal travel. Compare with that the increase of $\overline{7}$'s travel required in similar circumstances. Its shortest path to occupy the place of $\overline{6}$ (11 mm. medio-distal diameter) would be 25.7 mm., an increase of $1/14$ th on its normal travel to get into occlusion. So that unless there is a great acceleration of $\overline{7}$'s movement it will arrive in the place of $\overline{6}$ at a

Brash [2] shows the great forward movement of the teeth in the pig and considered it the chief method for obtaining room for the molar teeth. In four illustrations, two sagittal sections show new bone being laid down at the back of the roots of the teeth and at the alveolar margin. The other two pictures show a buccal and a lingual view of a mandible. A buccal view shows new bone laid down on nearly the whole surface right up to the anterior edge of the ascending ramus. A lingual view shows bone absorption, again up to the edge of the ascending ramus. The ascending ramus is being widened but not reduced on the anterior edge. All four pictures show bone being deposited at the posterior border, condyle and coronoid process. There is very little alteration at the lower border of the horizontal ramus, except reformation to keep its shape.

Humphry's [12] interpretation of his experiments appear to conflict with the evidence that I have brought forward from Broadbent's and Brash's work in respect of the growth of the mandible. In each of three experiments illustrated no doubt is entertained that bone is being deposited along the posterior borders. But the alteration on the anterior borders could be explained by deposit on the outer surface and absorption on the inner surface without any reduction of the anterior edge.

The following is clinical evidence of the normal forward movement of upper and lower teeth during the various transitional periods of the development of the dentition.¹

(1) Serial drawings of the upper teeth and the rugæ demonstrate that the teeth are moving forward in relation to the rugæ [11]. Brash (in a personal communication) showed that the bony rugæ of the palate of the pig are also moving forward during its downward and forward growth, so that the teeth must be moving forward through the bone at a greater rate than the rugæ.

(2) The occlusion of the deciduous teeth at 3 years of age is very definite. The cusps are sharp and the fossæ deep. The distal surface of $\frac{e}{e}$ are in the same vertical plane (fig. 3). From 3 years of age to 7 years the arches increase in size, the cusps of the teeth



FIG. 3.

FIG. 5.

become worn and the lower teeth move forward in relation to the upper teeth, so that the distal surfaces of $\frac{e}{e}$ are no longer in the same vertical plane but the lower is anterior to the upper. This allows $\frac{6}{6}$ to occlude correctly, i.e. the point of the medio-buccal cusp of 6 is a little in advance of the buccal groove of $\bar{6}$ but the triangular ridge which runs up from the point of the cusp disto-lingually is in the buccal groove [9].

¹ NOTE.—Dental symbols have been used to save space.

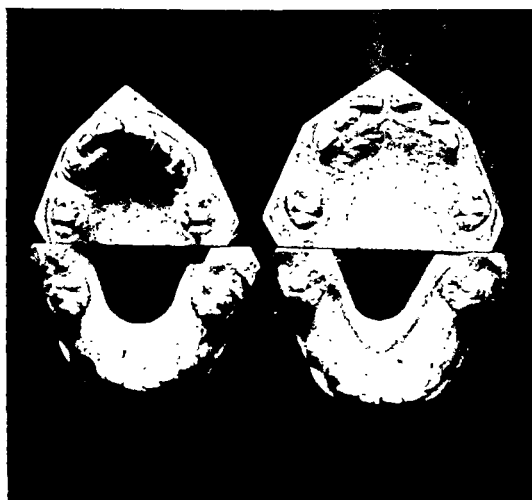


FIG. 7.



FIG. 8.

I propose to show a few extreme examples of migrations. The first two cases had $\begin{smallmatrix} e & d & b & a \\ \hline e & d & b & a \end{smallmatrix} \begin{smallmatrix} | \\ | \end{smallmatrix} \begin{smallmatrix} a & b & d & e \\ \hline a & b & d & e \end{smallmatrix}$ removed at 4 years of age owing to caries. $\begin{smallmatrix} c & | & c \\ \hline c & | & c \end{smallmatrix}$ were not a sufficient prop to keep the jaws apart and consequently the lower jaw swings upwards and forwards. When the incisors erupt the lowers are in front of the upper. One child was of deficient growth and the other approximately normal growth. The lag in forward growth of the upper incisal region is much more marked in the child with deficient growth (see figs. 7 and 8).

The third case, a normal growing child, had her $\begin{smallmatrix} e & d & | & d & e \\ \hline e & d & | & d & e \end{smallmatrix}$ removed at 6 and 8 years of age

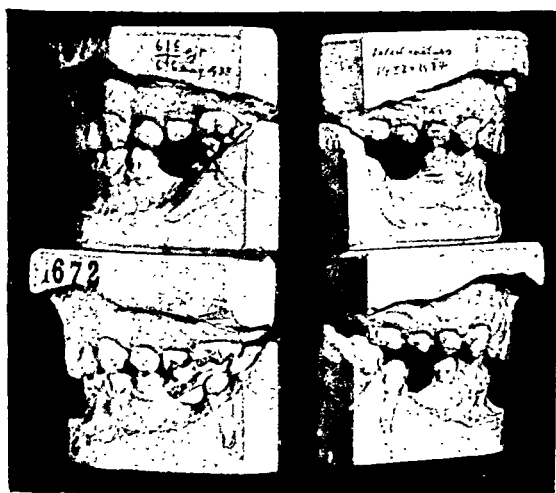


FIG. 9.

on account of caries. $\begin{smallmatrix} 6 & | & 6 \\ \hline 6 & | & 6 \end{smallmatrix}$ were removed at 11 years of age with the idea of prevention of crowding. The spaces in the upper arch have closed by the forward drift of $\begin{smallmatrix} 7 & | & 7 \\ \hline 7 & | & 7 \end{smallmatrix}$ which had rotated medio-lingually. $\begin{smallmatrix} 5 & | & 4 & 5 \\ \hline 5 & | & 4 & 5 \end{smallmatrix}$ rotated in opposite directions. In the lower jaw $\begin{smallmatrix} 5 & | & 5 \\ \hline 5 & | & 5 \end{smallmatrix}$ have been left behind in the forward growth as they develop so low down and had lost their guide, the roots of $\begin{smallmatrix} c & | & c \\ \hline c & | & c \end{smallmatrix}$ to bring them forward. They are

much later date than will $\bar{7}$ replace $\bar{6}$. My observation is that in fact it is upper teeth which are accelerated in eruption by premature loss of deciduous teeth or by loss of more medial permanent teeth. The effect of the very early replacement by $\bar{7}$ in the space of $\bar{6}$ as compared with replacing $\bar{6}$ is of course that any tendency for the crown of $\bar{5}$ to lag behind the root is early checked by the crowns coming into contact, whereas in the lower months or even years may elapse before $\bar{7}$ has made its extra distance, consequently the distal tilting of $\bar{5}$ has full scope to show maximum effect.



FIG. 4.

Salzmann [15] illustrates, (page 208) by courtesy of Broadbent, a case at 10 years and $13\frac{1}{2}$ years of age, where seven premolars are congenitally absent. $\bar{e}d$ and \bar{e} are present and there is a space between $\bar{3}$ and \bar{d} . When a line is drawn perpendicular to the Frankfurt plane from the registration point it is seen that \bar{e} and the teeth distal to it are moving forward and that $\bar{3}$ and the teeth medial to it are also moving forward. It is additional evidence of forward movement of teeth, but the fact that the crowns remain out of contact does not invalidate the proposition that crowns *tend* to lag behind when the growth of the bone is carrying the roots forward. That is clearly determined by the vigour of growth. Even in this case it is quite possible that the teeth in the anterior segment have lagged somewhat behind. The fact that the space for \bar{d} has almost disappeared makes it clear that the anterior teeth are not travelling forward as fast as the posterior.

I have tried to show the difference between the direction of growth in the upper and lower jaws and I think this difference will explain the varying behaviour of upper and lower migrations of molars and premolars following a break in the continuity of the arches. There is in addition a difference in the developmental position of upper and lower premolars [16]. The upper premolars are never far from the alveolar margin and the alveolar growth, owing to the small intervening space between the floor of the antrum and the alveolar margin. On the other hand $\bar{5}$ is developed very low down and if its predecessor \bar{e} is lost prematurely, the crown of the premolar can be left behind in the forward growth. The roots of the deciduous molars bring forward the crowns of the premolars.

There is also a difference of degree in the amount of forward movement of teeth anterior and posterior to a break in the arch due to normal or deficient growth of the child. In the normal growing child the anterior segment tends to keep growing and in some cases the posterior segment is not able to overtake it and close the space. In the child suffering from deficient growth, the anterior segment lags behind and the posterior segment rapidly closes the space. This has an important bearing on the prognosis of treatment of crowded incisors by the extraction of first permanent molars. In the child of deficient growth you get less relief in the incisal region and in the normal child, where relief is not so badly needed, you get more.

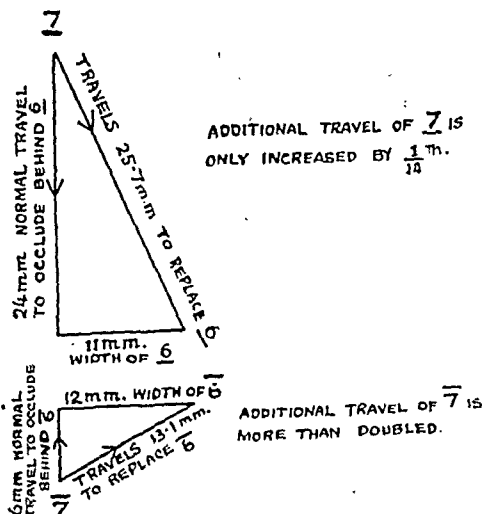


FIG. 6.

Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[February 8, 1945]

Injury to the Left Eyebrow Associated with Severe Visual Loss.—E. F. KING, F.R.C.S.

O. L., male, aged 35.

On 17.1.45 this man fell up some stairs. He was not unconscious and walked to hospital where stitches were inserted in a lacerated wound of the left eyebrow. It was not thought necessary to admit him to hospital.

I examined his eyes for the first time on 23.1.45, when he complained that his left vision had been defective since the accident. He gave no history of previous eye trouble and had never worn glasses.

On examination.—Right eye: Vision 6/6. Early macular degeneration, apart from which the eye was healthy. Left eye: Vision—counting fingers in lower field. Stitched lacerated wound in outer half of eyebrow. No irregularity of orbital margin. No displacement of globe and movements full. No mass palpable in the orbit. Pupil very sluggish on direct light stimulation; good consensual reaction. Media clear. Apart from slight macular degeneration, essentially similar to that present in the right eye, the fundus was normal. Field of vision: The only field present was in an area below fixation extending to the periphery. X-ray failed to reveal any foreign body or fracture of the orbit or optic canal.

When examined again on 2.2.45: Some improvement in central vision, now approximately 2/60. Slight relative temporal pallor of optic disc. Considerable extension of field of vision which now embraces fixation.

Observations.—It seems that this man sustained a hæmorrhage within the left optic nerve sheath. The points of note are: (a) The only external damage was to the skin of the eyebrow; there being no evidence of trauma to the eye itself. (b) An isolated area of vision in the lower field was all that remained following the injury. (c) The improvement in central vision and visual field which has been noted in the two weeks following the injury.

Duane's Retraction Syndrome

By Wing Commander A. J. ELLIOT, R.C.A.F.M.C.

Duane's retraction syndrome is characterized by deficiency of abduction, partial deficiency of adduction, retraction of the globe when the eye is adducted, oblique movement when adduction is attempted, narrowing of the palpebral fissure during adduction, and deficiency of convergence.

The syndrome was described in detail by Duane (1905) in a report of 54 cases of congenital deficiency of abduction with retraction, 5 of which were bilateral. He observed that the retraction of the globe may vary from 1 to 10 mm. on adduction. He felt that the retraction was due to the inextensibility of the external rectus muscle which failed to elongate and hence the internal rectus muscle could contract only by retraction of the eyeball. In 9 of the 54 cases the affected eye protruded slightly when adducted. He believed that the narrowing of the palpebral fissure was not a ptosis but it was due to the contraction of the orbicularis muscle, the closure being effected as much by an ascent of the lower lid as by a descent of the upper lid.

An atypical form of the retraction syndrome is the condition of strabismus fixus in which there may be a fibrosis of both the internal and external recti. Aebli (1933) reported 2 cases of this syndrome in which the internal rectus muscle was fibrous and attached to the globe at the equator.

The ætiology of the condition is not certain. It is not likely that it is due to a birth injury as Gifford (1926) reports a typical case of the retraction syndrome in an individual who was born by normal Cæsarean section. White (1944) considers that the condition is a congenital aplasia of the rectus muscle.

in contact with $\overline{7|7}$ leaving a large gap between the premolars (figs. 9, 10). It is a good example of the greater forward drift of upper molars compared to lower molars. In both upper and lower the anterior segments have kept growing forward and there is no marked reduction in the facial outline. In similar cases of deficient growth the anterior segments both upper and lower lag behind, the spaces close from behind and

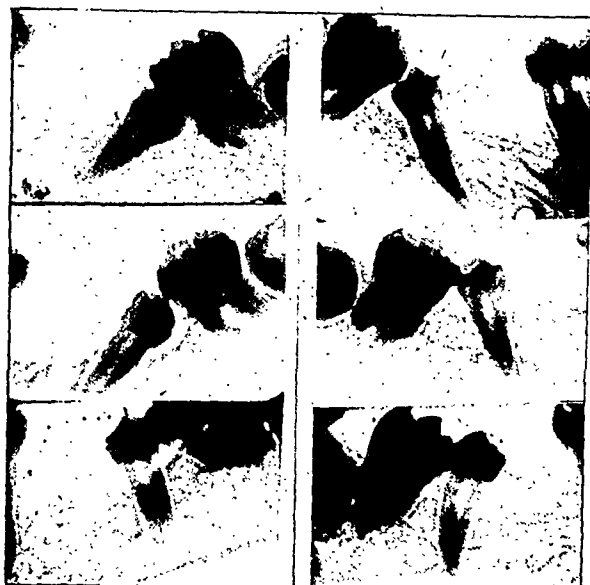


FIG. 10.

there is a very marked reduction in the facial outline. The radiographs show change of direction of $\overline{5|5}$ over a period of three years—no treatment.

SUMMARY

The evidence of normal growth and the development of occlusion show that all teeth are moving forwards. No evidence is available that teeth move backwards.

If spaces where teeth are extracted are closed, it is by drifting forwards of the teeth distal to the gap. Certain teeth, especially $\overline{5}$ after the loss of \overline{c} , can be left behind in the forward movement.

A difference in degree of forward movement anterior and posterior to a break in the continuity of the arch is observed in individuals with normal or deficient growth.

I am greatly indebted to Mr. H. T. A. McKeag of Queen's University, Belfast, for his help in this work.

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elevation and 30 degrees depression. With the eyes in the primary position the left eye was fixed outwards 15 degrees and slightly upwards. With the eyes turned to the left the left palpebral fissure was 3 mm. wider than the right. With the eyes directed to the right there was no adduction of the left eye which was markedly elevated underneath the eyelid. The left palpebral fissure was 2 mm. narrower in width than the right owing to the retraction of the globe.

A diagnosis of an atypical retraction syndrome was made in which there is a fibrosis of both internal and external recti, the degree of fibrotic replacement of the muscle fasciculi being greater in the internus.

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The Corrosion of Sharp-edged Ophthalmic Instruments. [Summary]

By J. FOSTER, C. H. LE MAY, and K. I. JOHNSTONE

EXTENT OF THE PROBLEM

E. F. KAYSER (Senior Technologist, Gillette Industries Ltd.) and one of us (J. F.) hope to read a paper at a later date showing that the extent of this problem is only revealed by optical control [40].

Kayser has shown by this method that: "Rusting may occur on the roughest part of a cataract knife (the ground zone) before use, when supplied ungreated, and that rust spoils edges (to a variable extent owing to marked variations in grinding) quicker than use".

Optical examination of sharp instruments ready for use at Manchester Eye Hospital (J. F.) showed 11.9% rejects of unused (2.6% on account of rust); and 47% of once or twice used (18% from rust alone; 17.6% from rust plus trauma).

A. *Corrosion in storage.*—Due to atmospheric water, salt, and acid, corrosion occurs on all ungreated knives, and is most marked in operating theatre cupboards, which have a water vapour tension equal to that of shops but a temperature 4.1° C. above them. This can be reduced by silica gel and lime desiccators, careful handling, and mineral grease. The comparative advantages of application of mineral grease by (i) melting, (ii) stable solvents, cf. CCl_4 and cyclohexane (not chloroform), or by oil ("three-in-one") are considered; (i) is most protective but (ii) safer to apply and remove.

B. *Antidotes to corrosion in sterilization.*—Rusting is worst on the ground zone, on curved edges and on high carbon steel. Although stainless steel of VDH¹ 750 exists [41] (and cataract knife steel has a VDH 760-810) it does not take a good edge (Kayser). Experimental knives and trephines of beryllium bronze proved moderate clinically and substandard by photomicrography.

Hot air sterilization [8, 16, 19, 38] is only slightly corrosive and kills spores, but is slow (half-hour at 165° C.) and requires a big outlay on the sterilizer and multiple sets of instruments. Hanne [17] found 17/18 sterilizers in Berlin inefficient from bad convection. Marchesani [24] claims five minutes at 180° C. to be adequate with his special sterilizer.

Hot mineral oil [1, 21] is non-corrosive, and produces complete sterility. It is slow (half hour at 150° C.) and difficult to remove. If vegetable oil is employed [10], each heating produces fresh corrosive fatty acids, gummy polymerization and oxidation products.

Chemical methods.—Alcohol [5, 21, 26, 35, 43] is useless [4, 44, 20], being corrosive (due to acetic acid and aldehydes) and will not kill even *Staph. aureus* at 130° C. in one hour.

Phenoloids (antiseptol) [2, 4, 8, 9, 15, 20, 21, 26, 28, 29, 30, 31, 32, 37, 43], Post's solutions, "Dettol", do not kill spores [9, 20], and require washing [8, 15, 28] or boiling to remove them prior to operation. Mercurials, e.g. Metaphen, attack aluminium and possibly steel. This is reduced by addition of borax [11]. Formaldehyde [7, 16, 21, 26, 32, 34, 43], cf. "Bard-Parker solution", and "Liquor sterilisans" [27] kill spores, but Burlingame says one to eighteen hours are needed if organic matter is present [34].

¹ Vickers Diamond Hardness.

No treatment is required if there is binocular single vision in the central part of the field of fixation. In cases where a disfiguring squint or diplopia is present the only treatment is surgical. Most commonly a moderate recession of the internal rectus muscle is indicated. However, the surgical procedure may be varied according to the findings in each case.

CASE REPORTS

CASE I.—C. W., a navigator in the R.C.A.F., aged 33, complained of blurring of near print after the use of the eyes for fifteen minutes.

On examination the vision was 6/5 in each eye without glasses. With the eyes in the primary position at 6 metres there were 30 prism diopters of esotropia; at 25 cm. there were 25 prism diopters of esophoria. The near point of convergence was 70 mm. The ocular movements showed limitation of abduction of the left eye to 35 degrees.

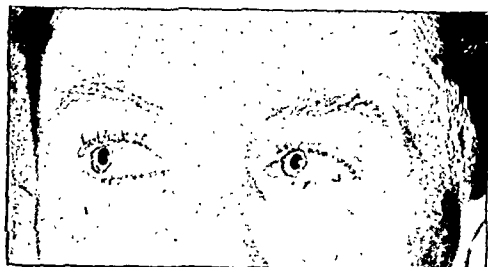


FIG. 1 a.

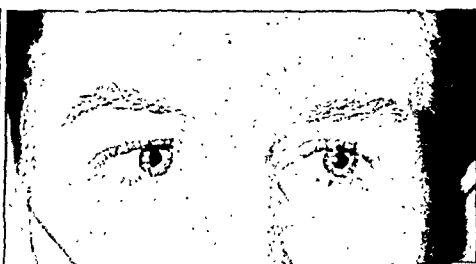


FIG. 1 b.



FIG. 2 b.

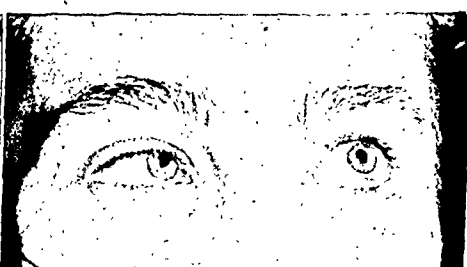


FIG. 2 c.

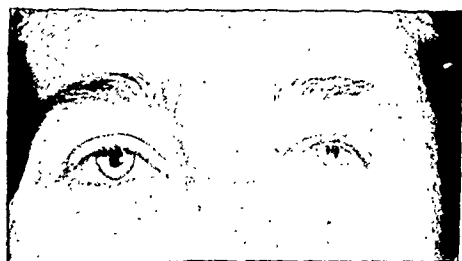


FIG 2 a.

FIG. 1 a and b (Case I).—Typical retraction syndrome.

FIG. 2 a, b and c (Case II).—Atypical retraction syndrome.

With the eyes turned to the right there was narrowing of the left palpebral fissure by 2 mm. and slight retraction of the left eyeball.

A diagnosis of congenital deficiency of abduction of the left external rectus was made. CASE II.—S. W., a clerk, aged 41, was examined in the clinic of Mr. Eugene Wolff, Royal Westminster Ophthalmic Hospital. She complained only of the cosmetic defect and stated that the left eye had turned out all her life.

On examination the vision with myopic correction was 6/6 in the right eye and 6/12 in the left eye. It was impossible to perform the cover test with the eyes in the primary position because the left eye could not be adducted to the median plane. The field of monocular fixation of the left eye revealed no adduction, 30 degrees abduction, 50 degrees

instrument; a 0.5% emulsion has been tried but leaves a soda deposit which is unpleasant to handle. The optimum may be determined by experience between 0.5% and 2%. For bare-handed operators the slipperiness is so slight as to present little inconvenience; for operators wearing rubber gloves it can be removed by wiping the instruments once with gauze before use.

The emulsion should be prepared by dissolving the soda crystals in a relatively small portion of the total water (distilled or well boiled), adding the AC.10 slowly with vigorous agitation to this concentrated solution to form a coarse concentrated suspension, which is then added to the remainder of the water. A fine homogeneous emulsion is formed when this mixture is boiled in the sterilizer.

The protection afforded by AC.10 is due to the inhibitor so affecting the relation between interfacial tensions in the metal-water-oil system that a film of oil—effective even if monomolecular—is *always* preferentially formed on the metal surface. In the course of sterilization, when the ebullition might interfere mechanically with the film, the special balance of its ingredients comes into play: the hydrophobic long-chain radical of the inhibitor molecules remains "anchored" in the oil while the polar sulphono-group is hydrophilic and permits the formation of an emulsion. Each "particle" of the boiling liquid therefore carries its own quota of AC.10 with it, and if the film on the instrument is disturbed it may be said to be replaced as rapidly as it is removed.

The effect of emulsifying AC.10 in the soda solution on materials other than metal used in surgical instruments is: *Ivory*—unaffected; *Silk* (experiments by Professor Speakman, University of Leeds)—not significantly affected; *Natural rubber*—elongation 10.5% after six hours' boiling—not significant in practice, but synthetic "rubbers" which would be totally unaffected could be substituted if desired; *Insulating varnish*—unaffected; *Glass*—refluxed for seventy hours—insignificant losses; *Aluminium handles*, unless dipped initially in neat AC.10, are slightly attacked by the alkali.

The AC.10 method permits sterilization by boiling, without corrosion, of all instruments for ophthalmic surgery rapidly and simultaneously in existing sterilizers.

As knives can be boiled for five minutes or more in 2% $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ without harm by the AC.10 technique, one of us (K. I. J.) determined whether protection of the cataract knife blade by immersion in AC.10 and subsequent boiling in an emulsion of AC.10 in sodium carbonate solution could be used to replace the customary boiling in a 2% solution of sodium carbonate (decahydrate) [6, 14], without invalidating sterilization.

Technique.—The blades were sterilized by flaming and each was dipped into a dense suspension of one of the following organisms in broth:

- Staphylococcus albus* (coagulase negative)
- Staphylococcus aureus* (coagulase positive)
- Bact. coli*
- Streptococcus pyogenes* (from a septicæmia)
- Pneumococcus* type 1
- Bacillus subtilis* (with spores)

After drying, the viability of the organisms on each blade was tested by making a small stab culture in an agar plate, or heated blood agar plate for the streptococcus and pneumococcus, using only the extreme tip of the blade. Only the pneumococcus failed to give growth in most experiments (see first line of the table).

Each blade was then dipped into (1) cold sterile AC.10 for fifteen seconds and (2) a 2% v/v emulsion of AC.10 in a 2% w/v solution of sodium carbonate (decahydrate) in distilled water, at boiling point, for five minutes, using a separate tube for each blade and for each reagent. Stab cultures were then made in duplicate with each knife, using the whole length of the blade. In every case the final stab cultures were sterile after incubation at 37° C. for eighteen hours (see the second line of the table).

To test for bactericidal action of the AC.10 and its emulsion, the experiment was repeated using tubes of emulsion at room temperature (see the third and fourth lines of the table). On *Staphylococcus albus* and *aureus* and on *B. subtilis* the AC.10 and its cold

THE STERILIZATION OF CATARACT KNIVES IN THE PRESENCE OF AC.10.

	Stab culture	Nutrient agar				Heated blood agar	
		<i>Staph. albus</i>	<i>Staph. aureus</i>	<i>Bact. coli</i>	<i>B. subtilis</i> with spores	<i>Str. pyogenes</i>	<i>Pneumococcus</i>
Sterilizing Experiment: Emulsion at boiling point	Initial	+	+	+	+	+	0
	Final	0	0	0	0	0	0
Control Experiment: Cold emulsion	Initial	+	+	+	+	+	0
	Final	+	+	+	+	0	0

+ = Growth.

0 = No growth.

As spores are only killed with certainty by formaldehyde amongst non-corrosive chemical agents, grease may interfere with their action and most of them require preoperative removal by aqueous washing or boiling, the method is not without disadvantages. Admittedly spore infection is rare, although recorded by Silberschmidt, Ulbrich, and Marchesani [3, 12, 18, 23, 36, 42], and corrosion is slight where exposure to water is minimal (Post's solutions [30, 31, 32], Dettol [9], and liquor sterilisans [21]).

Boiling water is a simple, detergent, complete and rapid mode of sterilization. All spores die in five minutes if 2% Na_2CO_3 [6, 14] is added to the water. Although the Na_2CO_3 reduces rusting by its alkalinity, some knives are spoilt in it by only half a minute's boiling [40] (a period lethal to all vegetative forms [25]). NaOH [45] and NH_4OH added to the water prevent rusting, but the risks of "carry-over" are too great. Chlorates, chromates, phosphates (by an effect analogous to "passivity") and nitrites reduce rusting.

Neutralin (0.073% NaNO_2 + 0.168% Na_2CO_3), which is used in dental sterilizers, is superior to Na_2CO_3 alone, and could be a useful addition to the "dipping" technique (no clinical trial) but will not preserve cataract knives for five minutes. Experiments with a mixture of Na_2HPO_4 and NaNO_2 are proceeding. Cathodic protection indicated directly by Woxén [45], and indirectly by Post [29] and Lancaster [22], has failed to protect razor blade edges experimentally (Kaysers).

High-frequency sound and electricity [33] are both possible fields for experiment, though the former is more successful with larger organisms, e.g. yeasts, and eddy currents [39] would require both inert atmospheres and special controls to prevent a rise above 200° C. and to avoid tarnish and "drawn temper" [12].

C. Corrosion in drying.—Knives last longer in Indian clinics owing to the generally alkaline air, immediate use on sterilization, and immediate drying after section by well-drilled theatre teams. We should copy them, as slow pre- and post-operative drying may cause rust as much as boiling.

Na_2CO_3 crystals on the blade produce surprising rust effects, and blood saline and Na_2CO_3 may produce a "cell" on the steel where they touch, and local pitting result. The knife blade, being thin, cools rapidly and therefore dries slowly.

A possible antidote to corrosion in all three stages may be found in "A.C.10 (Surgical)", described by C. H. Le May, B.Sc., of Manchester Oil Refinery Ltd.

"AC.10", the lightest of a series of anti-corrosive products developed as the result of many thousands of *ad hoc* experiments, consists of 95% of a light petroleum neutral oil and 5% of a complex of sodium salts of petroleum sulphonic acids (the "inhibitor"). Neither the oil nor the inhibitor alone is an effective corrosion preventive. To obtain optimum protection in a given set of conditions of exposure to corrosive attack, both the oil constituent and the mixture of sodium petroleum sulphonates must be carefully selected and mutually adjusted for compatibility. This is done by means of the experiments previously referred to.

"AC.10" itself was not originally prepared for protecting surgical instruments during sterilization; it was selected as the most likely of the existing range to satisfy the special conditions of this type of exposure, and its formula suitably adjusted to produce the modification known as "AC.10 (Surgical)"—referred to below as AC.10 for brevity.

In the case of AC.10 the oil can only be identified so far as an all-hydrocarbon body consisting, roughly, of paraffins—64%, naphthenes—31%, and aromatics—5%; the aromatics would fall in general within the range C_{20} – C_{30} . The inhibitor comprises the mixed sodium salts of petroleum sulphonic acids of average composition of the order $\text{C}_{21}\text{H}_{33}\text{SO}_3\text{H}$ – $\text{C}_{30}\text{H}_{39}\text{SO}_3\text{H}$.

Experiments checked by high-power microscopic examination showed: (1) That a cataract knife (1.55% carbon steel) if dipped for fifteen seconds in AC.10 can be kept indefinitely in water vapour, or water at room temperature, without rusting. This satisfies "storage" requirements. (2) That a cataract knife, first dipped for fifteen seconds in neat AC.10, can be boiled for 55 minutes in a 2% w/v solution of $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ in water in which 2% v/v of AC.10 has been emulsified, without corrosion. If it is re-dipped in neat AC.10 every fifteen minutes it can be boiled without corrosion indefinitely. This satisfies sterilization requirements.

After operation a sufficient film remains on the knife to protect it for a reasonable period before cleaning (fifteen to twenty minutes); after cleaning, the film should be renewed by dipping for fifteen seconds in neat AC.10 before putting the knife away for storage. Practical experience has confirmed that these results apply equally to all other sharp-edged ophthalmic instruments, and it is reasonable to conclude that they could be extended to all surgical instruments. The emulsion leaves a faint greasy film on the

instrument; a 0.5% emulsion has been tried but leaves a soda deposit which is unpleasant to handle. The optimum may be determined by experience between 0.5% and 2%. For bare-handed operators the slipperiness is so slight as to present little inconvenience; for operators wearing rubber gloves it can be removed by wiping the instruments once with gauze before use.

The emulsion should be prepared by dissolving the soda crystals in a relatively small portion of the total water (distilled or well boiled), adding the AC.10 slowly with vigorous agitation to this concentrated solution to form a coarse concentrated suspension, which is then added to the remainder of the water. A fine homogeneous emulsion is formed when this mixture is boiled in the sterilizer.

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As knives can be boiled for five minutes or more in 2% $\text{Na}_2\text{CO}_3 \cdot 10 \text{H}_2\text{O}$ without harm by the AC.10 technique, one of us (K. I. J.) determined whether protection of the cataract knife blade by immersion in AC.10 and subsequent boiling in an emulsion of AC.10 in sodium carbonate solution could be used to replace the customary boiling in a 2% solution of sodium carbonate (decahydrate) [6, 14], without invalidating sterilization.

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Sterilizing Experiment : Emulsion at boiling point	Initial	+	+	+	+	+	0
	Final	0	0	0	0	0	0
Control Experiment : Cold emulsion	Initial	+	+	+	+	+	0
	Final	+	+	+	+	0	0

+ = Growth.

0 = No growth.

emulsion had no effect, abundant growth being obtained in each final stab culture. *Bact. coli* gave irregular results, no growth being obtained in several experiments, due apparently to the action of the sodium carbonate *per se*. The streptococcus was killed in all cases at room temperature, whilst the pneumococcus rarely survived drying on the blade.

Two further lines of investigation were followed, being suggested by the above results, which are here only briefly reported:

(1) The rate of destruction of *B. subtilis* spores in the emulsion of AC.10 in sodium carbonate solution at its boiling point and in the separate constituents of the emulsion.

It was found that the spores of *B. subtilis*, a proportion of which will retain their vitality after boiling in water for ten minutes, are rapidly destroyed in the emulsion at boiling point, five minutes being adequate to attain sterility. The presence of sodium carbonate was essential.

(2) The bactericidal action of AC.10 emulsions for *Str. pyogenes* and the pneumococcus.

AC.10 as a 2% emulsion in distilled water is markedly bactericidal for the pneumococcus, less so for *Str. pyogenes*, and has no comparable action on *Staph. albus* or *aureus*, *Bact. coli* or *B. subtilis*. This bactericidal action is inhibited on the surface of heated blood agar.

CONCLUSION

Protection of inoculated cataract knives with A.C.10 and incorporation of AC.10 as a 2% emulsion in the 2% solution of sodium carbonate (decahydrate) in which such knives are boiled, does not interfere with sterilization, which is effected within five minutes for all organisms tested.

BIOLOGICAL REACTIONS OF AC.10

Professor Passey (Department of Experimental Pathology and Cancer Research, University of Leeds) arranged facilities for intensive instillation in the conjunctival sacs of rabbits for two weeks with a negative result, and added that the dilution and time factors would invalidate any remote effect from the irritant substances occasionally present in petroleum.

120 eye operations, including 25 cataracts, have been carried out successfully by this method, without reaction, since November 1944.

STERILIZER DESIGN

If the surgeon trying the method is disconcerted by the slight greasiness of the instruments, a separate compartment can be made in the sterilizer for AC.10 emulsion (for knives and keratomes only, in a small tray). One rub with sterile gauze brings all except molecular film off the handles, and a touch removes any excess from the blade. If the slight greasiness causes no inconvenience, or if there is time to rub each instrument separately, all can be sterilized together in existing sterilizers. Trays with a locking bar to hold instruments in order of use, and to serve simultaneously as a lifting fulcrum, are made to the design of one of us (J. F.) for both methods by Thackrays of Leeds.

ACKNOWLEDGMENTS

We wish to thank the following for advice, assistance, and laboratory facilities: Professors Whytlaw-Gray, Challenger, Speakman, McLeod and Passey, University of Leeds; Dr. Ulick R. Evans, University of Cambridge; Professor Loewenstein of the Tennent Institute; and the Directorate of Manchester Oil Refinery Ltd.

We regret that lack of space excludes photomicrographs and considerable experimental detail, but we hope to publish the paper *in extenso* at a later date in the *British Journal of Ophthalmology*. AC.10 can be obtained for experimental work from Down Bros., Weiss & Co. of London, and Thackrays of Leeds.

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Mr. G. H. Colt described how he had investigated this matter when he began practice in 1910. The microscopical examination of the edge of the blade did not truly indicate its sharpness for general surgical use. Neither did a method of determining the limiting friction through cheese prove any better guide. The man who sharpened the instruments for Messrs. Down Bros. taught him how to test the sharpness by cutting the surface epithelium of one's hypothenar eminence. This was much the best practical test. The borax solution referred to as having been introduced in 1937 was used extensively in those days for preserving purposes. It was invented by Mr. Lang of Moorfields about 1900. A special contrivance was also used for carrying the knives about in the bag but this was somewhat troublesome. With the new AC.10 it would work well. The older contrivance, which he exhibited, also had a locking bar like Mr. Foster's, but unfortunately it did not take the whole length of all the knives in use. It was also useful to be able to boil the silk, the instruments and the knives all together. The rotting of the silk by the soda solution depended to a great extent on the variety of silk used, and this led the late Sir Henry Gray to discard silk in favour of linen. Messrs. Down had made a shield for knives so that the edges were protected during boiling. It was obvious from the paper just given that such a method would not hold for the delicate work required from eye instruments without AC.10. The arrangement of which he was speaking was anything but foolproof. Unless shown, nurses would put the knives in the wrong way and so forth. But he found quite clearly that the blunting of knives was not due to the boiling (in general surgery), but to the protecting gauze rubbing against them and the actual contact with other instruments in the sterilizer. It seemed to him that the solution Mr. Foster had brought forward was likely to be of the very greatest use. Twenty to forty years ago it would have been advantageous to have it for the box-joints before rustless steel and chromium plating came in, for these joints always stiffened.

As regards skin grafting, any general surgeon who had the knack could cut large sheets of graft. All he needed was a really sharp knife and a flat piece of wood to stretch the skin, but he could not do it if the knife was in any way corroded. It had been his habit, in order to avoid possible infection coming back from the granulated surface, to dip the knife in the sterilizer on its way back to cut another section. Whether due to this practice or not, there had been no cross-infection by transmission from the one to the other and the edges had remained sharp.

Mr. Basil Graves said that the late Mr. Basil Lang used to emphasize the necessity of having the width of the blade of a Ziegler needle bear a correct proportion to the diameter of the shaft so that it would make a hole in which the shaft would fit easily yet would not allow aqueous fluid to escape. In order to ascertain the width of the blade in relation to the diameter of the shaft Mr. Graves had always put the instrument in Weiss's operating lamp, which was made so that it could be used as a lantern to project microscope slides, and this did reveal some features with regard to points and edges which, he would suggest, might at times be of use.

An Artery in the Canal of Schlemm

By EUGENE WOLFF, F.R.C.S.

THE vessel here described lies towards the posterior, i.e. the scleral-spur end of the canal of Schlemm.

It has a well-developed muscularis and is therefore an artery. It is some 60 μ in diameter and contains red cells, whereas the canal on either side of it appears empty.

The artery is surrounded by loose connective tissue which is not sclera, for its texture and staining properties are different. It stains in fact like that tissue which is normally found in varying quantity between the endothelium of the canal of Schlemm and the sclera.

Superficially this tissue meets the sclera, while on its deep surface it is continuous with the spongework of the ligamentum pectinatum (figs. 1 and 2).

The artery, therefore, lies in the canal and not in a partition between two portions of it. This may or may not be of purely histological interest. Followed in serial sections the artery is found to come from the anterior ciliary arteries. It is part of a circular vessel which runs parallel with the canal.

Maggiori, in his classical article, was the first to describe arteries as occurring normally in the immediate neighbourhood of the canal of Schlemm. This has been confirmed by Theobald and others. Maggiori figures a circular artery running close to, and parallel with, the canal, and some of his illustrations appear to show an artery actually in the canal.

The finding of an artery in the canal of Schlemm, therefore, should cause no surprise. It might quite well be that if the huge work of cutting complete serial¹ sections were undertaken an artery might be found in some portion of the canal in every globe. In any case it is part of the circular artery figured by Maggiori.

As to the significance of an arterial system of vessels in close relation to the canal of Schlemm, it seems probable that they may exist, since the sclera itself requires very little nourishment, for supplying those afferents to the canal to which Friedenwald has lately drawn attention.



FIG. 1.—General low-power view of the angle of the anterior chamber. Note the artery in the posterior part of the canal of Schlemm, and its relation to the anterior ciliary vessels.

¹ The artery here described was found during the routine examination of sections of an eye removed for a malignant melanoma of the iris, which, however, had nothing to do with its presence.

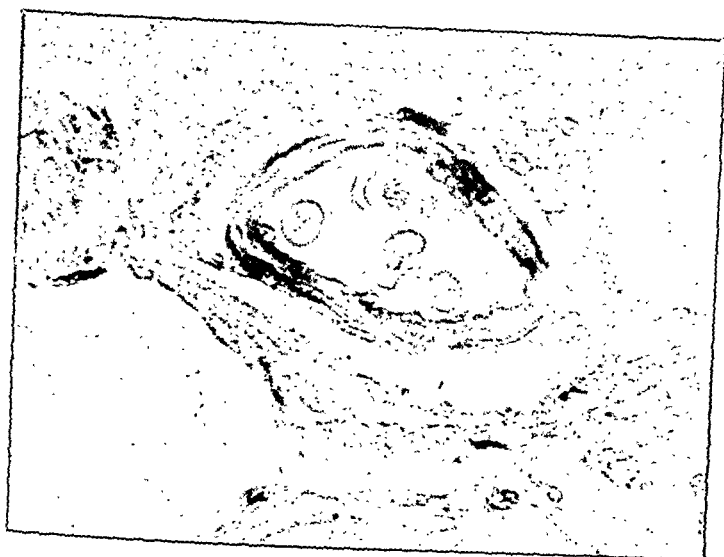


FIG. 2.—Under oil immersion (1/12th) to show the structure of the artery and its surround. $\times 750$.

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The Effect of Aluminium and its Alloys on Human and Rabbit Eyes. [Synopsis]

By L. H. SAVIN, F.R.C.S.

Mr. L. H. SAVIN said his interest in the subject was aroused by seeing, among the Dunkirk wounded, a number of eyes in which aluminium alloy fragments were embedded. He followed for three years the case of a young sergeant in whose only eye a fragment of aluminium zinc lay on the retina. The metal was at first bright and silvery. Later it became coated with a white cover of hydroxide. The fragment shifted twice, each time leaving a retinal "imprint", before eventually disintegrating into white powder. A second case behaved similarly.

Thirty-one implantations of aluminium and alloy fragments were made into the anterior chambers of rabbits by a standardized technique; and ten vitreous chamber implantations. There was no clinical difference in the behaviour of pure aluminium and various alloys tried in doses varying from 0.3 mg. to 20.0 mg.

The fragments were observed to become coated with white powder, with yellowish exudate, with fibrin, or in late cases with jelly. A late change often seen was powdering and fragmentation of the metallic fragment. In 6 cases the fragment was completely absorbed.

Common local changes were necrotic "imprints" left by the metal; of these 6 imprints were corneal, 12 on the iris (9 grey, 2 white, 1 necrotic), 2 in the lens, 4 in the fundus.

General effects on the eye included lens opacities in 28 eyes. Types of opacity included striae in 13 cases, 10 dots or vacuoles, 10 irregular opacities, and four cases with polychromatic lustre. Situation might vary: 5 anterior capsular instances, 6 anterior cortical, 2 capsular imprints, 3 complete cataracts, 4 posterior cortical.

Quiet inflammatory changes in the uveal tract were frequent. 10 posterior synechiae, 2 cases of iris bombe, and 14 cases of iris atrophy had been noted.

Other changes included pathological fundus pigmentation in 23 instances, 6 cases of localized choroiditis, 3 of retinitis proliferans. In order to obtain standardization of fundi initially, a special chinchilla: rex cross was bred. Partial coloboma of choroid was not uncommon in rabbits.

The artery is surrounded by loose connective tissue which is not sclera, for its texture and staining properties are different. It stains in fact like that tissue which is normally found in varying quantity between the endothelium of the canal of Schlemm and the sclera.

Superficially this tissue meets the sclera, while on its deep surface it is continuous with the spongework of the ligamentum pectinatum (figs. 1 and 2).

The artery, therefore, lies in the canal and not in a partition between two portions of it. This may or may not be of purely histological interest. Followed in serial sections the artery is found to come from the anterior ciliary arteries. It is part of a circular vessel which runs parallel with the canal.

Maggiori, in his classical article, was the first to describe arteries as occurring normally in the immediate neighbourhood of the canal of Schlemm. This has been confirmed by Theobald and others. Maggiori figures a circular artery running close to, and parallel with, the canal, and some of his illustrations appear to show an artery actually in the canal.

The finding of an artery in the canal of Schlemm, therefore, should cause no surprise. It might quite well be that if the huge work of cutting complete serial¹ sections were undertaken an artery might be found in some portion of the canal in every globe. In any case it is part of the circular artery figured by Maggiori.

As to the significance of an arterial system of vessels in close relation to the canal of Schlemm, it seems probable that they may exist, since the sclera itself requires very little nourishment, for supplying those afferents to the canal to which Friedenwald has lately drawn attention.

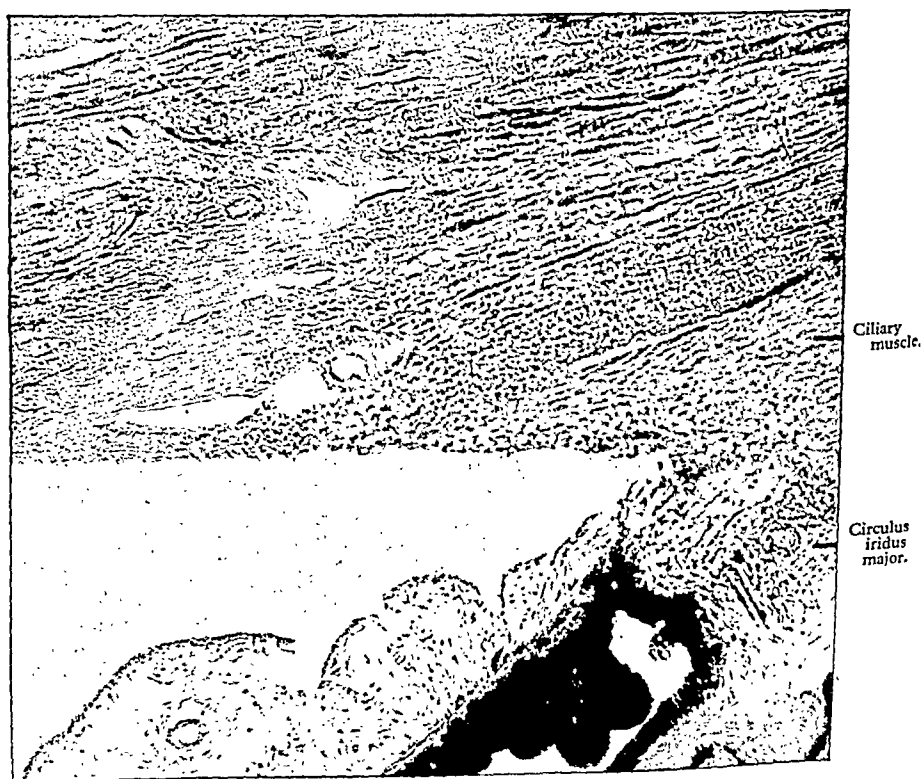


FIG. 1.—General low-power view of the angle of the anterior chamber. Note the artery in the posterior part of the canal of Schlemm, and its relation to the anterior ciliary vessels.

¹ The artery here described was found during the routine examination of sections of an eye removed for a malignant melanoma of the iris, which, however, had nothing to do with its presence.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[April 27, 1945]

Diphtheria Antigens—Their Preparation, Properties, Laboratory Testing and Statutory Control. [Abridged]

By Sir PERCIVAL HARTLEY, C.B.E., M.C., D.Sc., F.R.S.

AN outstanding event in the diphtheria field in the inter-war period has been the clear demonstration that individuals and communities can be protected by active immunization. Medical research has provided the diphtheria prophylactics by means of which this is achieved. This period has also seen the establishment of the Therapeutic Substances Act, and, for its administration, the Medical Research Council's Department of Biological Standards at Hampstead has provided biological standards and has examined samples of therapeutic substances, including diphtheria prophylactics, controlled under the Act for compliance with statutory requirements.

In 1907 Theobald Smith advocated the use of toxin-antitoxin (T.A.) for the active immunization of man, and in 1913 von Behring reported the results of the first trials of T.A. in children. The six years time-lag is not easy to understand, as it was well known that these mixtures of T.A. would immunize animals: it was probably due, in part, to a reluctance to inject children with materials which were toxic to guinea-pigs and, in part, to the absence of any simple test to determine which members of a community should be immunized and what the results of such immunization might be. von Behring's demonstration of the safety of T.A., and Schick's description of his famous test in 1913 cleared the way for the practical application of T.A. on a wider scale. Progress in Germany was impeded by the war of 1914-18, but in 1913 in America, Park's energy and enthusiasm and his unwavering faith gave active immunization a start from which it has never looked back. In 1921 Glenny, Allen and O'Brien described T.A. and the Schick test and advocated their practical use, and later in the year Copeman presented a Report on Diphtheria to the Ministry of Health; and in December Copeman, O'Brien, Eagleton and Glenny described the use of the Schick test in a school at Mitcham, the successful immunization of the susceptibles with T.A. and the number and nature of the local reactions produced.

At the time, little was known of the composition of von Behring's T.A., but Park described these materials and their properties fully. Much research was given by these early workers to the discovery of the best toxin-antitoxin mixture for use in man. A very precise adjustment was essential; if too much antitoxin was added the mixtures were ineffective antigens and if too little they might be unduly toxic and even dangerous. Whether the right balance had been struck, whether the permitted toxicity had been exceeded, and whether the mixtures were effective antigens was determined by injecting prescribed quantities into guinea-pigs. In this way laboratory control of the materials was instituted and later incorporated in the regulations made in the United States and Great Britain and afterwards in other countries for the control of these antigens.

These toxin-antitoxin preparations of von Behring and Park started a great movement, but their chief defect was that they contained toxin and, although this was combined with antitoxin and presumably effectively controlled, they were potentially dangerous and accidents followed their use—at Dallas, Concord and Baden in the early days, and later in other countries. Although there had been no accident in this country (and, as a matter of history, there never has been any accident of this kind in England) nevertheless, for some years before it became obsolete, every batch of T.A. was tested, for safety and antigenic potency at Hampstead before it was released for use.

Glenny has always maintained that *toxoid* and not *toxin* should be the basis of all diphtheria antigens and he first applied this guiding principle to T.A. In 1923 he and Hopkins reported the successful immunization of man with *toxoid*-antitoxin mixture—a preparation which was to gain renown as T.A.M. This is easier to prepare than T.A., since the precise adjustment of *toxoid* and antitoxin is of less account, and if a little

Pathological vascularization occurred often; there were not enough controls to decide whether the reaction was specific for aluminium.

Among other oddities were noted 2 cases bullous keratitis, 1 staphyломatous eye (false buphthalmos), 2 cases of zonular keratitis, 1 interstitial keratitis, 1 deep keratitis, 2 pigmented cornea, 1 pigmented limbus, 2 folds in Descemet's membrane. These were interesting but statistically unimportant.

Histological changes were mostly what would be expected from the clinical appearances. Attempts were being made to trace the aluminium through the tissues by special dyes.

Altogether it was definite that aluminium was by no means inert as supposed by some previous observers. In these cases the experimental fragments had been probably left insufficiently long.

Dacryocystorhinostomy: A Simplified Method. (Film.)

By T. M. TYRRELL, F.R.C.S.

In introducing the film Mr. Tyrrell said it was not intended to cover the whole operation from end to end, but only to show the main points of the operation. These were: (i) The incision was a long one to give a good exposure. (ii) The operator attempted to remove the lacrimal bone in one piece by three blows with the hammer and chisel. (iii) No attempt was made as in other operations of this nature, to preserve the nasal mucosa, as it was not used in this operation to make the anastomosis. (iv) The patency of the anastomosis was assured by repeated syringing over a long period.

Mr. Tyrrell did not wish to advocate this as a superior operation to those already practised, but wished to point out that it had the great advantage of speed as it could be done easily in ten minutes, provided that one used some form of sucker to control bleeding.

The anæsthesia was 5% novocain with adrenaline for the skin and tissues down to and including the periosteum. For the nasal mucosa, the nose was first sprayed with 20% cocaine and then a pledget of wool on an orange stick was pushed up the nose armed with cocaine and adrenaline paste.

Cocaine hydrochloride	..	dr. 2
Desiccated suprarenal gland (5 in 1)	gr. 24	
Chlorbutol	..	gr. 5
Paraffin liq.	..	min. 220
Paraffin moll. or alb.	..	to 2 oz.

Discussion.—In reply to the President, Mr. Tyrrell said he left the sac quite free without attempting to stitch it to the nasal mucosa.

Mr. E. F. King asked if the results had been good in the contracted grossly infected sac.

Mr. Tyrrell replied that to date the results had been fairly good, he would estimate about 50% for this type of case. He added that he removed a piece of the nasal wall of the sac corresponding to about two-thirds of the size of the hole in the nasal mucosa.

Mr. O. Gayer Morgan said that he had used Mr. Tyrrell's technique of removing the lacrimal bone and applying a hole in the sac to a hole in the nasal mucosa but his results were much better since he had used a sutured anastomosis. The film showed what a splendid exposure of nasal mucosa was obtained and it seemed a pity to cut it off and waste it. In a successful anastomosis no after-treatment was required as no contraction by fibrous tissue took place.

Mr. Lindsay-Rea said that he remembered watching Granström in Stockholm splitting the posterior surface of the lacrimal sac from top to bottom and sewing into the edge of the sac a flap of nasal mucosa in order to create a large permanent opening. Referring to Mr. Tyrrell's method of keeping the opening into the nose patent by frequent syringing he thought that the presence of a style night and day for some time would probably be better. Mr. Lindsay-Rea congratulated Mr. Tyrrell on his cinema picture taken in colour which demonstrated his technique most beautifully.

Mr. J. F. Simpson said that he had done a fair number of these operations. He did not make the incision as high as the one shown in the film, because the important part of the anastomosis was at the lower end of the sac, the incision being made along the whole length of the available sac to include this part. He had found no difficulty in carrying it out in the active stage of suppuration. If the suturing was carefully done there would be no need for any probing or washing through afterwards. He did not touch the patients after the operation unless they still watered. The anterior flap of both nasal mucous membrane and sac was sometimes more difficult to get together in textbook fashion than the posterior. He agreed that failure to form the flaps did not always preclude a successful outcome, but it practically always obviated any after-treatment when they had been properly sutured.

known all over the world as A.P.T. The preparation and purification of the toxin and toxoid, and the A.P.T. prepared from it, and the different stages of manufacture have been systematically investigated at the Wellcome Laboratories and, in its modern form, A.P.T. is a relatively pure antigen, slowly absorbed from the tissues, not liable to cause local reactions especially when used for the first immunization of young children. It contains no antitoxin and therefore does not sensitize to horse protein. Its greatest merit is that it is effective in two doses while all other forms require at least three injections. Opinions differ as to whether, and when, the Schick test should be performed in a campaign; but most would agree that, if it is to be omitted, it is with this antigen that this could be done with most justification.

Experiments were described to show the effect of delayed absorption of the antigen. Guinea-pigs injected with highly purified diphtheria toxoid dissolved in saline did not become immunized; while those injected with the same dose of the same antigen mixed with 1% starch solution developed antitoxin. The object had been to find a substance which would combine the advantages of alum and be without some of the defects which alum appeared to possess in the early stages of its use for this purpose. The explanation of the results is on the basis of the observations of Glenn, Buttle and Stevens, who showed that toxoid is rapidly eliminated; and in the immunological behaviour of the insoluble antigens like T.A.F. and A.P.T. The interest of the experiments is that starch or some similar bland, innocuous, non-antigenic colloid might perhaps be used to modify, or prolong or intensify biological activity of other antigens, or of other substances like penicillin, for which alum and other similar substances may be inapplicable.

In this country progress in the active immunization of man against diphtheria has received setbacks due to fatal accidents in other lands, following the injection of diphtheria antigens. At Dallas in 1919, at Concord in 1924, at Baden in 1925 children died following the injection of what should have been perfectly safe toxin-antitoxin but which, because three different mistakes had been made, were preparations containing diphtheria toxin in amounts lethal for human beings. These tragic accidents created a profound impression in this country, but they strengthened the resolve that every step should be taken to prevent an occurrence of this kind in the United Kingdom; and they brought support for a scheme then being developed which had for one of its objects the security and protection of the doctor who administered, the patient who received, and the manufacturer who prepared, modern remedies of this type. The war of 1914-18 had shown the need for controlling the manufacture and testing of arsenicals of the arspenamine type, measures for which had been successfully improvised during the war. The inaccessibility of the unit for diphtheria antitoxin during the war had been an embarrassment; the discovery of insulin had emphasized the need for action; the extreme variability of the potency of pituitary extract, the infection of vaccine lymph with tetanus in the United States, these recurring accidents with diphtheria antigens, the discovery of new remedies and the whole trend of medical research, all made it clear that the supply of materials of this kind should not be left to the uncontrolled activities of any well-meaning but inexperienced person inclined to try his hand; or, it may well be, to the charlatan and the quack in this or any other country. These are highly specific remedies, many of them potentially dangerous, dependent for their benefit, to the patient on precise dosage, nearly all required to be administered by injection, and accordingly required to be sterile, all of them calling for technical skill of a high order and wide experience for their proper manufacture and testing.

The Therapeutic Substances Act of 1925 was the result. By this Act, diphtheria prophylactic can only be prepared by accredited licensees, and licences are only granted to those who can reach and maintain the very high standard demanded as to expert staff, laboratories, plant and equipment. Moreover, all preparations of diphtheria prophylactic must conform to the standards of purity, potency and quality laid down, and these standards are designed to secure for the doctor and his patient the best that industry and research can provide. Obviously, with these powers the provision of diphtheria prophylactic can be brought under very effective control.

The author then went on to discuss in some detail the question of the control of the antigenic potency of diphtheria prophylactics. The requirements of the schedules, their defects and limitations and the consequence of these, the bases for revised regulations and the results achieved by these in practice were described. The consequences which followed the attempt to assess potency by simply observing the animal reaction following their injection were pointed out, while at the same time the difficulties in the way of carrying out this assay in direct comparison with a standard preparation were set out. It was shown that antitoxin production in the guinea-pig—on the basis of which the potency of prophylactics is at present assessed—is due, among other things, to the

toxin remains in the toxoid this is taken care of by the antitoxin added. Moreover, only one-half to one-third of the toxoid need be neutralized with antitoxin, giving the equivalent of an under-neutralized mixture which is of practical advantage; and the preparation is absolutely safe. T.A.M. has been superseded in recent years, but it played a useful part in the early days and it has an honourable record.

That diphtheria toxin can be deprived of its toxicity by formalin is a very old observation ascribed to Salkowski in 1898, rediscovered by accident at least twice and repeatedly confirmed by later workers. Glenny, Lowenstein and Ramon also showed that these formol-toxoids are remarkably efficient antigens. Used first for the immunization of animals, Glenny and his colleagues suggested that this product could be used for the immunization of man and about this time the results of Ramon's work were published. Ramon's great contribution in this field includes two achievements with which his name will always be associated; he gave to science the application of the flocculation reaction whereby quantitative measurements of toxin and antitoxin could be made by *in vitro* methods, and he persuaded the French authorities to immunize large sections of his countrymen, particularly its children and its soldiers, against diphtheria. For many reasons—ease of preparation, freedom from sensitizing horse protein, its property of flocculating with antitoxin, its safety and its field performance—formol-toxoid has enjoyed a wide popularity and in many countries besides France and Canada it is the antigen of choice. Its drawback, reckoned a serious one in England, is that it is liable to cause unpleasant local reactions especially in adults. It is possible that, in this respect, formol-toxoids prepared in some countries are less likely to produce local reactions than in others. However, it must be conceded that some of the most outstanding achievements in mass immunization have been won by formol-toxoid.

Park had been faithful to toxin-antitoxin, and American workers had naturally followed his distinguished leadership, but in late 1923 or early 1924 he was on the way to conversion to the use of formol-toxoid. His interest was aroused when O'Brien sent him some formol-toxoid prepared in the Wellcome Laboratories with the request that he would test it. This Banzhof did in animals and Sawhill in nurses; and very shortly afterwards Zingher reported some excellent results obtained in man with formol-toxoids prepared in New York. These tests were concluded just about the time that the mishap at Concord occurred (January 1924) and Park was not slow to realize that formol-toxoid had advantages over toxin-antitoxin; and later he admitted that the practical results following its use were in no way inferior.

In 1923 it was shown that the precipitate which forms when toxin and antitoxin are mixed together, and washed free from broth constituents, is a very active antigen; that practically the whole of the activity of a mixture is contained in the precipitate; that the nitrogen content of the washed floccules is very low, and that the antigenic activity of a floccule preparation is directly related to the composition of the mixture from which it separates (Hartley). This antigen was prepared later in Germany. Being highly purified it causes little or no reaction on injection.

Toxin-antitoxin floccules suffered from one of the main defects of toxin-antitoxin, viz. it contained toxin and this constitutes a source of potential danger, although possibly a remote one. However, in 1927 Glenny and Pope showed that the floccules prepared from mixtures of toxoid and antitoxin possess all the virtues of toxin-antitoxin floccules and are completely safe. Thus T.A.F., toxoid-antitoxin-floccules, became available for the immunization of man in 1927, and it has established itself as one of the two antigens commonly used in this country at the present time. It owes its popularity partly to the fact that it causes so little local reaction and thus is particularly suitable for the immunization of adults; and partly because of its effectiveness, giving high Schick conversion rates as a rule; e.g. in 1942, Freeman reported a Schick conversion rate of over 99% with over 700 children immunized with the T.A.F. in Islington. The efficiency of T.A.F. is due to its insolubility and slow absorption, the effective immunization being due to the long-continued stimulus thus provided.

Experiments were described to show that antitoxin production by T.A.F. in guinea-pigs is much slower than by formol-toxoid and that six weeks after injection it is only one-quarter of that at twelve weeks. This may explain why T.A.F. appears to be a less potent antigen than toxoid, and also why its performance in man exceeds its promise as judged by tests on guinea-pigs. It is clearly inadmissible to test floccule preparations in comparison with a formol-toxoid standard: with the latter, maximum production of antitoxin occurs about three weeks after injection and declines rapidly.

In 1926 Glenny and his colleagues showed that when alum is added to formol-toxoid an insoluble precipitate is produced which has high immunizing properties. This was first shown for animals which were injected with the whole mixture of toxoid and alum. For man much purer products have been prepared and the antigen has come to be

known all over the world as A.P.T. The preparation and purification of the toxin and toxoid, and the A.P.T. prepared from it, and the different stages of manufacture have been systematically investigated at the Wellcome Laboratories and, in its modern form, A.P.T. is a relatively pure antigen, slowly absorbed from the tissues, not liable to cause local reactions especially when used for the first immunization of young children. It contains no antitoxin and therefore does not sensitize to horse protein. Its greatest merit is that it is effective in two doses while all other forms require at least three injections. Opinions differ as to whether, and when, the Schick test should be performed in a campaign; but most would agree that, if it is to be omitted, it is with this antigen that this could be done with most justification.

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diet administered; it was shown that, all other things being constant, guinea-pigs given mangolds do not grow, do not all survive and do not all immunize while those given cabbage, grow, live and immunize very easily. It was also shown that the same antigen, examined by the same method in different laboratories, in fact, under conditions in which the guinea-pig is the only variable, produces widely different quantities of antitoxin. As in the case of other biological products these difficulties could only be overcome by the adoption of a standard preparation in terms of which the potency of another sample could be estimated by means of comparative tests. The possibility of applying these principles to the assay of diphtheria prophylactic had been explored at Hampstead, and some of the results so far obtained were described. Even with the admittedly uniform stock of guinea-pigs there maintained it was shown that the individual variation in the response of guinea-pigs to antigenic stimulus was quite large and, in consequence, the errors of the assay must be large. These errors had been determined in relation to the number of guinea-pigs used in the comparative tests.

A standard had been provisionally adopted for the assay of A.P.T. at Hampstead and the results of its application in two field investigations, which had been made possible by the co-operation of Professor G. S. Wilson and his collaborators, were described. The results yielded by the first of these had been of value in deciding the requirements which a batch of A.P.T. must fulfil before it is brought into use: these are, first, that the sample must contain not less than 50 flocculation units per c.c., and, secondly, that under certain prescribed conditions the geometrical mean of the antitoxin produced by 10 guinea-pigs must be not less than 2 units per c.c. This field experiment showed that the samples which produced 2 units per c.c. or more gave a highly satisfactory Schick conversion rate, while those which produced less than this amount gave a low rate. In the second experiment, in which manufacturers' samples conforming to the above requirements were studied, the standard and the maker's sample were compared for their field performance in children, and the potency of the maker's sample in terms of the standard preparation was determined at the Hampstead laboratory. A table was shown summarizing the results of these field and laboratory tests.

(The paper was illustrated by photographs of the pioneers in this field and by lantern slides recording the results of the experiments described in the text.)

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The following took part in the discussion: Dr. R. A. O'Brien, Dr. A. T. Glenny, Dr. H. J. Parish, Dr. Hewitt, Dr. J. A. H. Brincker and Mr. L. B. Holt.

Clinical Section

President—J. D. ROLLESTON, M.D.

[February 9, 1945]

Sudden Onset of Tachycardia and Arrhythmia. Paroxysmal Auricular Tachycardia with Atrio-Ventricular Block. ? Mitral Stenosis.—A. SCHOTT, M.D.

Male, aged 42. Complains of fatigue and dyspnoea and palpitation on exertion.

Family and previous personal history non-contributory.

Graded A1, October 1942. Arrived in France in August 1944 in perfect health. His duties consisted in carrying and filling petrol cans which he was able to do without any difficulty. In October 1944 he caught a "heavy cold" with slight cough, but carried on with his work. About five days afterwards he developed in the evening a sudden attack of very marked shortness of breath with a choking sensation and substernal pain. He collapsed in his biller, but did not lose consciousness. On the following morning he reported to the M.O. who sent him to hospital with a diagnosis of mitral stenosis and auricular fibrillation. Subsequently the diagnosis of mitral stenosis was upheld by some observers, rejected by others; aortic valvular lesion also was suspected on radiological grounds. At times auricular flutter was diagnosed. In spite of digitalis treatment tachycardia persisted throughout; the heart action at times was regular, at times irregular.

1.12.44: Admitted to Guy's Hospital.

Attention is drawn to the absence of any rheumatic history or of previous complaints pointing to a cardiac lesion, the sudden onset, the absence of any murmur pathognomonic of mitral valvular disease and to the radiological features: absence of a typical mitral shape of the left border, enlargement of the heart shadow to the right and enlargement of the left auricle in the postero-anterior view. On one occasion enlargement of the left auricle in the right oblique view also had been reported, but subsequent examinations at Guy's Hospital failed to confirm this.

Electrocardiograms showed the arrhythmia to be due to paroxysmal auricular tachycardia with A-V block. Large doses of digitalis first slowed the auricular rate from 300 and over to 250 and then to a rhythm rapidly varying between sinus rhythm with and without coupling and idioventricular rhythm with coupling, the last probably associated with block between the impulse-forming centre and the auricles. Some special features of paroxysmal tachycardia with A-V block (as distinct from the common form without A-V block) were discussed, in particular the fact that this form tends to occur more frequently in diseased hearts, that the attacks tend to be much longer than those of the ordinary form and that they are far more resistant to treatment (see Barker *et al.*, 1943; Decherd and Herrmann, 1944; and Decherd, Herrmann and Schwab, 1943).

The question of the presence of a mitral valvular lesion can only be decided after radiological re-examination at a time when normal rhythm has been present for some time since similar arrhythmias are known gradually to produce enlargement of the auricles even in the absence of a valvular lesion, although only after a much longer time (e.g. auricular flutter, see Kossmann and Berger, 1941).

Grateful acknowledgment is made to Dr. A. H. Douthwaite, under whose care the patient was admitted to Guy's Hospital, for kind permission to demonstrate the case and publish his notes.

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Dr. Wilfred Stokes did not think that this was a case of mitral stenosis. Clinically there was no murmur, the mitral first sound only being split. Alternating extrasystoles, one understood, may have been caused by digitalis; but, as certain of the electrocardiograms only showed evidence of auricular tachycardia, with A-V dissociation in CR, the auricles might still be in abnormal rhythm. Accordingly, the absence of murmurs did not exclude mitral stenosis with certainty.

From the X-ray appearances, mitral stenosis was improbable because there was not the slightest increase in the conus accompanying the definite enlargement of both auricles.

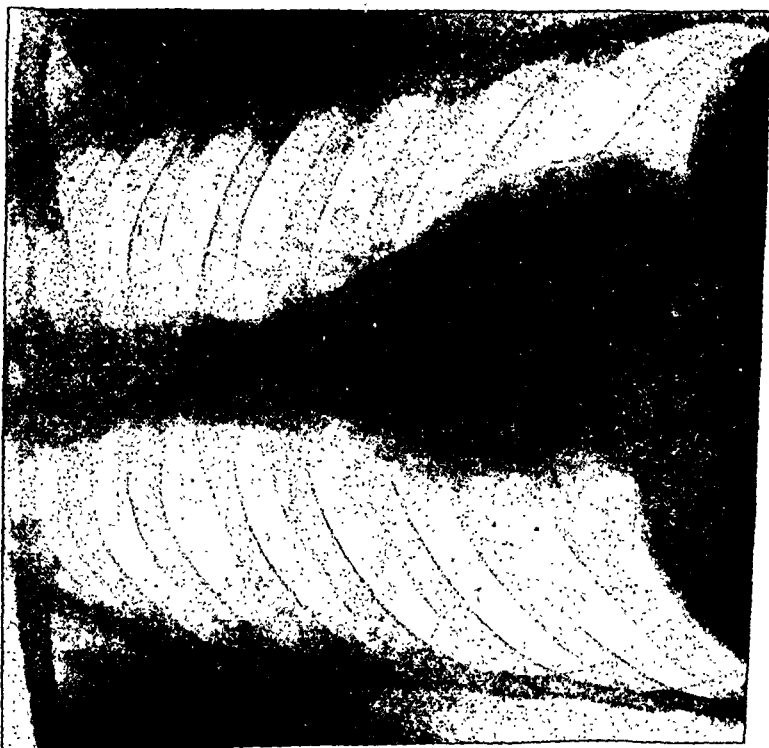


FIG. 1.—Teleroadiograph of chest. Note enlargement to the right and shadow of the left auricle inside shadow of the right auricle.

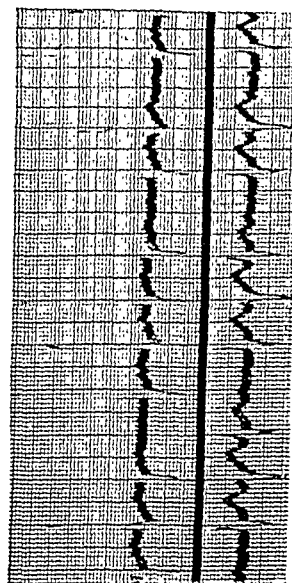
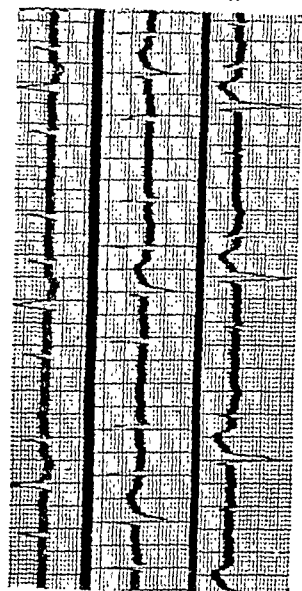


FIG. 2.—Record taken January 26, 1945. After one week on tinct. digitalis, minims 15 t.d.s. Paroxysmal auricular tachycardia with A-V block. Note absence of P waves in leads 1 and 2, indistinct P waves in leads 3 and IVR. Only in lead CR are the P waves sufficiently distinct to make a diagnosis possible. Auricular flutter can be excluded by the presence of an isoelectric interval between the P waves. Note also the different shape of the T waves of the supra-ventricular beats following an extrasystole (see Scherf, 1944). Auricular rate between 300 and 330.

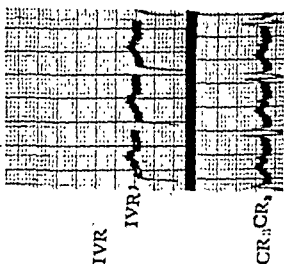
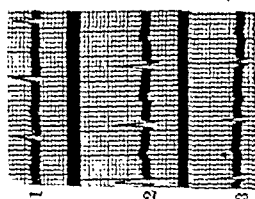


FIG. 3.—January 30, 1945. After one week on tinct. digitalis, minims 15 t.d.s. and subsequently minims 15 q.i.d. for three days. Auricular rate 250, 2:1 block. Only lead CR makes the diagnosis possible.



FIG. 4.—January 31, 1945. After another day of tinct. digitalis, minims 15 q.i.d. Auricular rate unchanged at about 250. Varying 4:1 block.

Dr. Stokes favoured the suggestion that auricular enlargement was caused by prolonged arrhythmia of those chambers, and suggested cardioscopic observation at intervals after normal rhythm was regained.

(Since the meeting a paper with close bearing on this subject has been published—"The unity of paroxysmal tachycardia and auricular flutter," Evans, W. (1944) October, Brit. Heart J., 6, 271.)

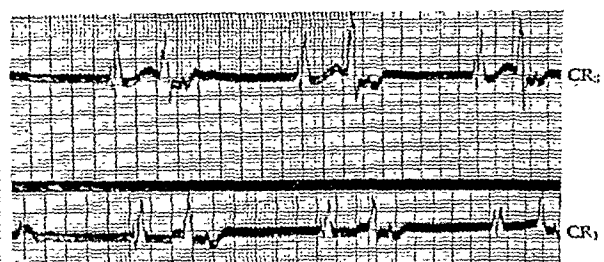
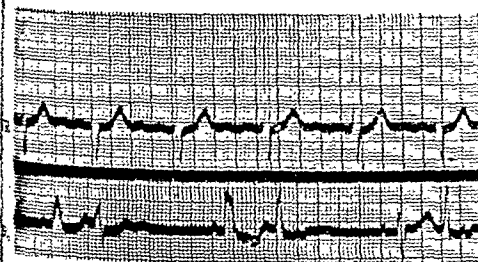
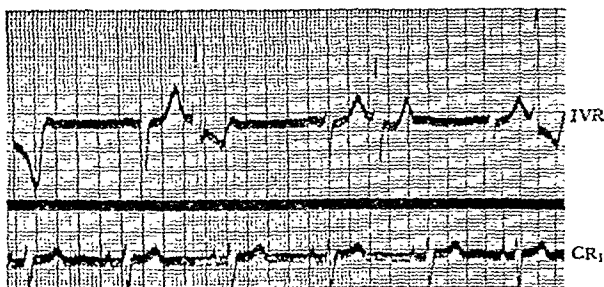
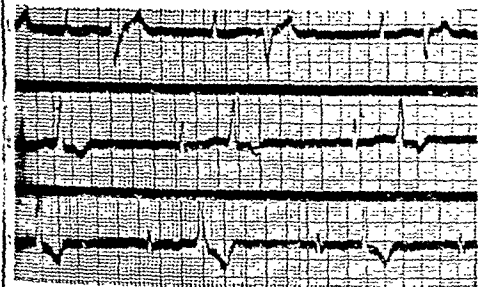


FIG. 5.—February 7, 1945. After a total dose of tinct. digitalis, 15 i.d.s. for one week and min. 15 q.i.d. for the subsequent 20 days, with clinical signs of overdosage. Record obtained 20 days after discontinuing digitalis. Sinus rhythm with coupled beats in leads 1, 2, 3 and CR₁; in lead IVR probably sinus rhythm with a rate of about 70. Note alternating lengths of the P-P cycles, the P-P intervals containing ventricular complexes being considerably shorter than those without them.

FIG. 6.—February 8, 1945. Limb leads (not shown): sinus rhythm with and without coupling. IVR: sinus rhythm with coupling. CR₁, upper strip: sinus rhythm, rate about 60. CR₁ and CR₂ (lower strip): idioventricular rhythm with coupling, ? block between impulse-forming centre and auricles; ? retrograde conduction.

Pulsating Exophthalmos.—A. DICKSON WRIGHT, M.S.

Mrs. M., aged 57, fell heavily, striking the back of her head and was momentarily stunned but did not vomit. The following day she was aware of a vibrating noise in the centre of her head which gradually grew stronger and eventually prevented sleep. The swelling of the right eye was noticed on the third day and increased rapidly so that on her admission it was very unsightly, proptosed, chemotic, congested and painful and pulsing with the heart beat. There was still some movement of the globe and the fundus showed engorged veins and hæmorrhages. With the stethoscope a loud bruit could be heard which ceased on pressing the carotid in the neck. The blood-pressure was 200/90 and the pulse of the Corrigan type. Twelve days after the accident the internal carotid was tied. Although three hours' occlusion with a clamp had preceded nevertheless five minutes after the closing of the ligature the patient became hemiplegic and aphasic (she was left handed). The ligature was quickly removed and speech and movement returned.

Seven days later the less drastic common carotid ligature was done after a preliminary injection of the cervical sympathetic chain with novocain. No complications occurred, and the patient recovered normally. Unfortunately in the week between the two ligatures the sight and movements of the eye had been lost although the eye is rapidly returning to normal appearance.

? Aplastic Anæmia Treated by Splenectomy.—MAURICE SHAW, D.M., and L. C. OLIVER, F.R.C.S.

Gordon, D., aged 54, builder. First seen on 15.6.44 complaining of "rheumatic pains", dyspnoea on the slightest exertion, œdema of the ankles and lassitude for the past two months. Appetite had been poor for six months and he had lost 1½ st. in the past year.

History.—Previous health good except for gout in 1940 and "rheumatism" in 1942.

Family history.—Nothing relevant.

On examination.—Well covered but with marked pallor of the skin and mucous membranes. No glands palpable but spleen moderately enlarged and liver easily palpable. Haemorrhages present in both optic fundi. Slight oedema.

Blood-count.—Hb. 28%; R.B.C. 900,000 per c.mm.; C.I. 1.5; leucocytes 1,800 (polys. 53%, eosinos. 1%, basos. 1%, myelos. 4%, metamyelos 5%, lymphos. 34%, monos. 2%).

On admission to hospital (29.6.44) gastric analysis after histamine showed complete achlorhydria. Myelogram, after sternal puncture: myelos. 15%; metamyelos. 12%; polys. 16%; basos. 1%; lymphos. 1%; megaloblasts 28%; normoblasts 27%. Reticulocytes approximately 10% of non-nucleated red cells. Van den Bergh reaction—Direct: very delayed weak positive. Indirect: 2.5 mg. per 100 c.c.

A diagnosis of primary aplastic anaemia was made. He was treated with plexan, anahæmin and pentide and received 9½ pints of blood by intravenous transfusion. By these means his blood improved to Hb. 38%; R.B.C. 1,660,000; leucocytes 2,400.

Operation.—It was then decided to try splenectomy which was performed by Mr. L. C. Oliver on August 18. As all available veins had been used up by previous transfusions, preparations were made for an arterial transfusion. Towards the end of the operation the anaesthetist reported rapid deterioration in the patient's condition and a pint of blood was given directly into the abdominal aorta. The patient made an uneventful recovery except for some thrombosis in the veins of his legs associated with a rise in the platelet count to 1,126,000. He was discharged from hospital on September 28.

Report on spleen (Dr. R. G. Waller): The spleen is enlarged and weighs 700 grammes. The histological appearances, apart from diffuse hyperplasia, are not abnormal. The microscopical picture does not conform to that of acholuric jaundice.

The latest blood-count (26.1.45): Hb. 88%; R.B.C. 3,800,000 per c.mm.; C.I. 1.1; leucocytes 13,000 (polys. 60%, eosinos. 3%, lymphos. 8%, monos. 29%). Red cells show a moderate anisocytosis and a slight degree of polychromasia. Two nucleated red cells seen in 100 white cells. Platelets 435,000.

[March 9, 1945]

Cyst-like Calcification in Left Ventricle.—COURTENAY EVANS, M.D.

C. F., male, aged 57. Five months' history of cough and sputum. Breathless attacks occurred at night, lasting twenty minutes; these were relieved by coughing. Two months



FIG. 1—Calcification in left ventricle. Right oblique view.

FIG. 2—Anterio-posterior view.

ago he became short of breath on walking a hundred yards. There was no pain in the chest; cough slight.

Past history.—Not significant, he has not been abroad.

Examination.—Pale man. Heart not enlarged, no congestive signs. No valve defect, rhythm regular. B.P. 150/96. Few sibili heard over chest. Abdomen normal. Urine

normal. Circulation time (arm to tongue) 16 seconds. Haemoglobin 100%. Sedimentation rate 1 mm. in one hour. Blood W.R. negative.

Electrocardiogram: T₁, T₂, T₄ inverted, deep Q₄. Absent R₄. S or Q waves in leads 2 and 3.

Radiography shows an oval calcified shadow lying in the left side of the heart, probably in the substance of the left ventricle (figs. 1 and 2).

Treatment with a potassium iodide and stramonium mixture and ephedrine tablets has relieved symptoms. Rest and digitalis did not have any beneficial effect.

Dr. A. Elkeles: Calcification may occur in a cardiac aneurysm, but this is usually associated with enlargement of the affected ventricle and a characteristic ventricular bulge can often be observed in the radiograph. In this patient the size and the shape of the heart are within normal limits and the cyst-like calcification is within the border of the left ventricle, which is confirmed by X-rays taken in the right and left oblique positions.

Calcification may also take place in chronic constrictive pericarditis, but in this condition a rim of calcium is visible along the periphery of the heart and does not produce an oval-shaped, cyst-like appearance. The calcified shadow in this patient might be caused by one of the very rare tumours of the heart; it resembled a case of "Calcified cyst of the pericardium" published by Mr. Dickson Wright (1936, *Brit. J. Surg.* 23, 612).

The possibility of a hydatid cyst may be considered in differential diagnosis.

Aortic Regurgitation, with Evidence of Stenosis of Innominate Artery.—A. L. JACOBS, M.R.C.P.

Mr. J. A., aged 43. Boarding-house manager (formerly engineer).

History.—At 10 years: "Acute rheumatism" (six months in bed). At 23 years: Acute appendicitis. At 36 years: Rheumatoid arthritis. From 1938 to 1940, five times in hospital for this. At 41 years: Bronchopneumonia.

Present complaint.—Increasing dyspnoea and frequent anginoid attacks for six months. Admitted to Paddington Hospital 17.2.45.

Cardiac signs from previous hospital records—1938: Apical systolic murmur. 1940: Aortic diastolic murmur. 1943: Aortic systolic and diastolic murmurs, Corrigan pulse.

Present condition.—Severe dyspnoea at rest. No systemic congestive signs.

Heart.—Great left ventricular hypertrophy; arrhythmia (dropped beats, irregular in incidence); loud aortic systolic and diastolic murmurs. No thrill.

Vessels.—Radial: Left, pronounced Corrigan pulse; right, the pulse upstroke appears much less sharp. Subclavian: Left, very forcible Corrigan pulse; right, long thrill. Carotid: Left, slight thrill; right, long thrill. Arterial blood-pressure: Left arm, 175/40; right arm, 155/40.

Joints.—Rheumatoid arthritis, residual deformities.

Skigram.—Extreme left ventricular enlargement. No obvious saccular aneurysm.

E.C.G.—Extreme left axis deviation; partial A-V block (P-R interval 0.36 sec., dropped beats); S-T₁ and S-T₂ depressed, T₁ and T₂ inverted.

Pulse tracings (Dudgeon).—Left: Sharp upstroke and pronounced pre-dirotic notch; right: Slight anacrotic wave, no pre-dirotic notch.

Blood reactions.—1940: W.R. negative, G.C.F.T. positive; 1943: W.R. negative, Kahn R. negative; 1945: W.R. negative, Kahn R. negative. After provocative dose of 0.3 gramme N.A.B. 6.3.45: W.R. negative, Kahn R. negative.

Diagnosis.—The main interest of this case lies in the aetiology. The development of the aortic lesion after the age of 38 years, the anginoid attacks and the evidence of involvement of the orifices of the great arteries support a diagnosis of specific aortitis. On the other hand there is no general aortic dilatation, the blood W.R. has been persistently negative and there is a history of rheumatic fever during childhood. The electrocardiographic changes might be accounted for by either aetiology. The aetiological question is further complicated by rheumatoid arthritis.

Dr. Wilfred Stokes suggested that not too much attention should be paid to the history of rheumatic fever. With such gross inequality of the radial pulses he favoured the diagnosis of syphilitic aortitis.

Cervico-Facial Actinomycosis. Penicillin Therapy.—E. C. B. BUTLER, F.R.C.S.

Woman, aged 54. Three months' swelling of the left side of her face and jaw; a tooth was removed and she was treated as an osteomyelitis of the lower jaw.

23.1.45: Transferred to Claybury Emergency Hospital. There was an indurated swelling round the angle of the lower jaw with many sinuses. X-ray showed no bony disease. Culture of the pus (Dr. Valentine): Actinomycosis. Penicillin-sensitive.

7.2.45: 120,000 units of penicillin given intramuscularly every day for a total dosage of 2 million units.

9.3.45: All sinuses healed, no pain, no pyrexia and very little induration left.

This patient had no specific therapy except penicillin. Her surgical treatment consisted in draining superficial collections of pus from time to time. The immediate response to penicillin therapy was very good, and even if there is a relapse at a later date healing occurred much more rapidly than is usually the case.

Comment.—Since the introduction of chemotherapy it has been increasingly obvious that there are many pathogenic strains of actinomyces. We have found some which are sensitive to penicillin, others to propamidine and some to gentian violet. This immediately opens up fresh fields for local and systemic therapy. In the past our treatment consisted in a course of potassium iodide working up to 200 grains a day for many weeks; drainage of any obvious abscess followed up by a course of radiotherapy.

A small series of 20 inframandibular infections all recovered under this treatment and were well when followed up from six months to three years. Healing, however, often took over six months. Since the introduction of penicillin we give systemic penicillin to those cases which are sensitive; in others injection of propamidine jelly or gentian violet into the sinus appears to shorten the duration of the infection. Radiotherapy is still of value. Propamidine is also very efficient in destroying secondary infection with hæmolytic streptococci if present.

Potassium iodide is now no longer given as a routine procedure. We have not found that the sulphonamides gave any permanent benefit, possibly because their action may only affect the secondary infection which is nearly always present.

Carcinoma of Lower End of Œsophagus. Radical Resection with Œsophagostomy by a Left Transpleural Approach.—IVOR LEWIS, M.S.

Mrs. A. C. M. Housewife, aged 56. Admitted to North Middlesex Hospital July 14, 1944.

History.—Always had good health until a month before admission, when she noticed some difficulty in swallowing which was not very serious. No loss of weight. She was seen by Mr. F. D. Cairns, who diagnosed carcinoma of œsophagus and referred her as probably an operable case.

On admission.—A short, alert, healthy-looking woman, who can still swallow most ordinary food with little difficulty. Fairly fat. Clinical examination negative.

Investigations.—X-rays (Dr. Holdsworth): Carcinoma involving lowest 2 in. of œsophagus (fig. 1). Œsophagoscopy (I.L.): Exuberant neoplasm lower end of œsophagus (at 30 cm.—a short patient). Histology (Dr. H. Rogers): Adenocarcinoma.

Operation (July 19, 1944).—Left transpleural œsophagectomy with œsophagostomy, in one stage. Anæsthetic (Dr. Faux): Endotracheal tube, closed circuit ether and



FIG. 1.—Mrs. A. C. M., showing carcinoma of cardia.

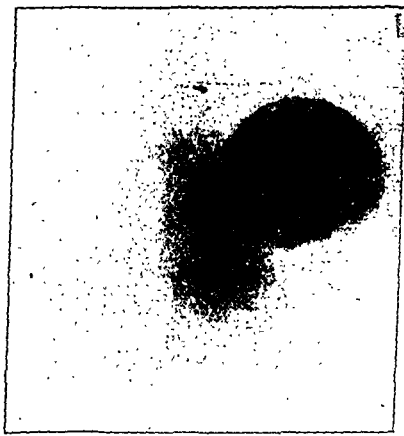


FIG. 2.—Mrs. A. C. M., showing anastomosis in left thorax.

oxygen, respiration "controlled" during latter half of time. The left 8th rib from neck to cartilage was removed. The lowest 2 in. of œsophagus was a solid cylinder of growth, areolar tissue outside condensed but not adherent. Using "guy-ropes" of tape, the distal œsophagus was dissected free as far as aortic arch. The diaphragm was then divided radially and the stomach brought up into left pleura. A wedge of cardia was resected with œsophagus and gap in stomach closed. A gastric bed was then made along posterior mediastinum up to the arch of the aorta. This was securely sutured in place, the

oesophagus laid on it, and then an end-to-side anastomosis performed using interrupted, fine silk sutures, closely placed, throughout in two layers. A few sutures were inserted in the diaphragm but so that a finger could still be passed alongside. An intercostal catheter was connected to a waterseal bottle. Two pints of blood were transfused during operation. Condition at end of operation was very good. Pulse 84.

Progress.—Two days after operation she started regurgitating some "black fluid" every time she coughed, which proved to be stale blood and gastric contents (16 oz. residue) and caused some anxiety. It appeared that the post-operative oedema was enough to occlude the hole left in the diaphragm. It was treated by gentle suction and washing out through Ryle's tube twice a day. On the fifth day, to spare her veins, a jejunostomy was done under a local anæsthetic and the opportunity taken to feel the gap in the diaphragm. It was not unduly tight. However a large catheter was passed up into thoracic stomach, with its lower end in duodenum. This helped to keep the dilated upper chamber drained till the stomach regained its tone. The gastric contents steadily became cleaner, the emptying was studied by small barium swallows and as soon as it was satisfactory—on the ninth day—she was allowed to take fluids (fig. 2). The drainage from the pleura was only 3 or 4 oz. in all and the intercostal tube was removed after two weeks as the discharge was clean. The jejunostomy tube was taken out after three weeks. She got up on the seventeenth day.

Her wounds healed by first intention. Discharged on August 20, 1944, taking full ordinary diet, the only injunction being to avoid hard or too bulky food.

She has remained very well with no night regurgitation. She does her ordinary housework.

Carcinoma of the Oesophagus. Radical Resection with Oesophagogastrostomy for a Midthoracic Growth by a Right Transpleural Approach.—IVOR LEWIS, M.S.

P. R., a metal-polish worker, aged 66, was admitted to North Middlesex Hospital on August 4, 1944.

History.—Always a healthy man until four months before admission, when he began to get difficulty with swallowing.

On admission.—A wasted, rather pale man, who could only swallow fluids.



FIG. 1.—P. R., showing carcinoma mid-oesophagus.



FIG. 2.—P. R., X-ray April 13, 1945, showing oesophagogastrostomy in right thorax.

Investigations.—X-ray: Neoplastic stricture of middle third of oesophagus at the level of the bronchus (fig. 1). Oesophagoscopy (I.L.) August 5, 1944: A carcinomatous stricture at 32 cm. papilliferous, reasonable lateral mobility. Histology: Squamous carcinoma.

Operations.—I. August 7, 1944: Preliminary laparotomy. No secondary spread. Therefore the upper half of the stomach was mobilized. A Witzel jejunostomy with a 12 catheter completed this short operation. By August 20 he was unable to swallow anything.

This patient had no specific therapy except penicillin. Her surgical treatment consisted in draining superficial collections of pus from time to time. The immediate response to penicillin therapy was very good, and even if there is a relapse at a later date healing occurred much more rapidly than is usually the case.

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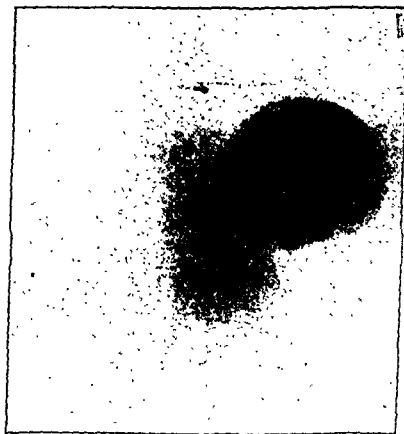


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Section of the History of Medicine

President—SIR ARTHUR MACNALT, K.C.B., M.D.

[March 7, 1945]

Robert Hooke, M.D., F.R.S., with Special Reference to His Work
in Medicine and Biology¹

By HENRY W. ROBINSON,
Librarian of the Royal Society.

ROBERT HOOKE was born on July 18, 1635, at Freshwater, Isle of Wight, where his father was the minister of the parish. He was educated at Westminster School and at Christ Church, Oxford. Whilst at Oxford he worked for Robert Boyle, for whom he built an air-pump and carried out many experiments with it. It was also at this time that he made many trials with a pendulum and formulated his theories regarding the motion of the planets. It was Boyle who introduced Hooke to the Royal Society and in 1662 he was made Curator of Experiments, a post he held until his death. Thus began the association with the Royal Society and the responsibility of regularly conducting experiments for the Society. There can be no doubt that Hooke was the one man who did most to shape the form of the new Society and to maintain its active existence. Without his weekly experiments and prolific work, it could scarcely have survived, or at least, as to the beneficial results of the appointment on Hooke's own development. His occupation almost forbade a systematic investigation of any one problem. He had to serve a group of men of widely varying interests, many of whom were merely dilettantes seeking amusement, all of whom had an insatiable curiosity in almost any and every aspect of natural phenomena. During the next forty years he accomplished a vast amount of work and was responsible for innumerable brilliant experiments. It is true that many of his researches were inconclusive but his occupation partly explains the reason for much of his work being left uncompleted.

In the year following his appointment as Curator, Hooke was elected a Fellow of the Royal Society and was exempted from all charges. Later in the same year, he was made responsible for keeping the Society's repository in Gresham College. About the same time Sir John Cutler offered Hooke £50 a year to deliver lectures at Gresham College. In 1664 he was elected Gresham Professor of Geometry in succession to Isaac Barrow. During the Great Fire of London and while the ruins of the City were still burning, Hooke produced a model for the replanning of London, apparently with a "chess-board" street plan. The model does not survive, but, like all the other ideal plans produced, it was found impracticable as soon as a preliminary survey of the ruins had been made. This, and Hooke's obvious abilities, led to his appointment on October 4, 1666, as one of the Surveyors for the City.

¹ Illustrated by slides kindly lent by Professor E. N. da C. Andrade, F.R.S., Dr. E. A. Underwood and the Royal Institution.

II. August 28, 1944: Transpleural œsophagectomy under ether and oxygen anæsthesia, intratracheal tube, CO₂ absorber (Dr. Faux). The right 6th rib was removed. The growth was found to extend from just below the vena azygos major for 2½ in. distally. Several lymphatic glands were involved. The gullet was dissected free down to the diaphragm. The cardia and fundus and finally four-fifths of the stomach, with attached omentum, were brought up into the right pleural cavity. The œsophagus from vena azygos to cardia was resected and the gap in the stomach closed. After preparing a "gastric bed" to take the œsophagus, and fixing it securely high up along the posterior mediastinum with multiple sutures, the stump of the gullet was anastomosed end-to-side to the fundus. Condition at the end of operation was good.

Progress.—Two days after operation some œdema developed at the bases, which cleared up after a pint of concentrated blood serum. (Blood protein had fallen to 5.5%.) For the first fortnight he was only allowed sweets or ice by mouth. The jejunostomy was ample for his sustenance—he was getting milk and glucose, 4 to 6 pints a day, by this route. From the second day a Ryle's tube was passed into his stomach, daily, the contents aspirated and gently washed out. On the fourteenth day he began feeds by mouth, increasing steadily as gastric emptying was shown to be good by X-rays. He was allowed to get up from the seventh day and was walking downstairs and into the garden on the twelfth day. The intercostal drain gave no trouble and was left out at the end of two weeks. There had been only slight infection by *B. pyocyaneus*. On discharge he had a good appetite, was able to eat anything without discomfort and was putting on weight. Condition now good, has gained 34 lb. (fig. 2). No regurgitation.

[*Note.*—It is hoped to publish elsewhere an account of this new procedure for carcinoma of the mid-œsophagus.]

Excision of the Parotid Gland with Preservation of the Facial Nerve. Three Cases.—

H. A. KIDD, F.R.C.S.Ed.

(1) Mrs. A. F. G., aged 53. Admitted 5.11.43. Hard tumour in upper part of parotid, not circumscribed. History of a swelling in right side of face for one year, gradually increasing in size; swelling and pain.

9.11.43: Gland resected under intratracheal gas, oxygen and trilethylene (Dr. Helen Barnes), and a rubber tissue drain inserted for forty-eight hours.

Convalescence uneventful, but there was a considerable degree of facial palsy. A facial splint was applied and electrotherapy given. Complete recovery in six months.

Report on section (Dr. Roland John): Lipomatosis and atrophy of parotid and salivary gland.

(2) Mrs. E. R., aged 44. Admitted 31.12.43 with history of nine weeks' swelling in the parotid; no pain on mastication. Tonsillectomy in 1930. Swelling of the upper cervical glands had preceded the occurrence of the tumour.

On examination.—A very hard, fixed swelling in the position of the pre-auricular gland, about the size of a cherry. B.P. 180/100. Chest X-ray: Negative for tuberculosis. Cervical glands not enlarged.

At operation (4.1.44) a tumour the size of a hazel nut was found in the substance of the parotid, and the whole gland was completely excised. The wound was drained and convalescence was uneventful.

On section the tumour contained thick green pus. Report (by Dr. Roland John): (1) Caseous tuberculosis of lymphatic glands lying in relation to serous salivary gland. (2) Slight fatty atrophy of otherwise normal serous salivary gland.

The caseating gland belonged to the intraparotid group, and was in relation to the external carotid artery. Facial paresis was present after operation, but responded to the same treatment as Case (1).

(3) Mrs. L. W., aged 39. Admitted 29.1.44, complaining of a swelling which had been present since influenza just after Christmas. The tumour had been increasing in size, was tender on pressure and fixed. Cervical glands not enlarged; occasional rise of temperature to 99%. Chest X-ray negative for tuberculosis, but the condition was thought to be tuberculous.

Operation (1.2.44) under pentothal, gas, oxygen and chloroform (Dr. Mittell): Gland excised and facial nerve dissected out. Wound was closed with drainage. During convalescence there was some pyrexia which responded to M & B 760.

Patient discharged 12.2.44. Similar after-treatment to that of previous cases. Complete recovery.

Report (Dr. Roland John) (Sections 1, 2) Subacute inflammation of parotid salivary gland. (3, 4) Subacute inflammation of lymphatic glands.

This case would, very probably, have recovered without operation, but in view of the history, operation was thought to be advisable if the facial nerve could be preserved.

Similar remarks occur almost daily throughout the Diary. Of particular interest are his references to the illnesses of Bishop Wilkins (Bishop of Chester), Sir Robert Moray and others.

On November 16, 1672, he reports: "Lord Chester desperately ill of the stone, stoppage of urine 6 days. 4 red-hot oyster shells quenched in a quart of cyder and drank was advised by Dr. Glanvill. Dr. Goddard advised blisters of cantharides applied to the neck and feet or to the veins." And two days later: "At Lord Chesters, he was desperately ill and his suppression continued", and on the following day he recorded that the Lord Bishop of Chester had died about 9 in the morning of a suppression of urine. Two days after that he says: "Dr. Needham brought in an account of Lord Chesters having no stoppage in his urters nor defect in his kidneys. There was only found 2 small stones in one kidney and some little gravel in one ureter but neither big enough to stop the water. Twas believed his opiates and some other medicines killed him, there being no visible cause of his death." Regarding Sir Robert Moray, Hooke tells us on July 4, 1673: "This evening Sir Robert Moray died suddenly being choked with flegme in endeavouring to vomit." He had died at Lord Chancellors and about an hour before his death drank 2 glasses of cold water. On the following day he wrote: "Sir Robert Moray's face taken off, his body opened by Sir Charles Scarborough at the King's command. Found very entire and sound and nothing amisse and no visible cause of his death." Perhaps, he, too, died through taking too much medicine. Here are other short extracts from the Diary: "At Sir Jonas Mores, sick, he was cured of a sciatica by fomenting the part for an hour with hot steams, afterward chafing in oils with a rubbing hand and heated firepans, which gave him sudden ease." "Sir Theodore Devaux told me of Sir Thomas Mavens' cure of stone in kidneys by blowing up bladder with bellows." "Mrs. Tillotson told me that an ounce of castile soap boiled in a pint of ale till the ale was half consumed and drank warme was a sure medicine for the yellow jaundice, which had been often tried with certain effect."

And now to pass on to the work which Hooke did in biology and medicine. He achieved less in these fields than in any other branch of science, but what he did do undoubtedly added to the knowledge of his contemporaries and has been of some importance and help for later generations. The improvement he made in the construction of the microscope, and the work he performed with the aid of it, led to some of his most important discoveries. He attached a field or middle lens to the microscope and made other minor improvements. With this microscope he made numerous observations and communicated them to the Royal Society. In 1665 he published them in a volume entitled *Micrographia, or Some Physiological Descriptions of Minute Bodies made by Magnifying Glasses*. This is the first important book on the microscope and the first to give drawings made from objects under the microscope. The following passage from the preface to his book will emphasize the difficulties with which Hooke had to contend in making those remarkable drawings, especially when we remember the very poor lighting that was available: "I endeavoured first to discover the true appearance and next to make a plain representation of it. This I mention because of those kind of objects there is much more difficulty to discover the true shape, than of those visible to the naked eye, the same object seeming quite differing in one position to the light, from what it really is and may be discovered in another. And therefore I never began to make any draught before, by many examinations, in several lights and in several positions to those lights, I had discovered the true form. For it is exceeding difficult in some objects, to distinguish between a prominency and a depression, between a shadow and a black stain, or a reflection and a whiteness in the colour. The eyes of a fly in one kind of light appear almost like a lattice, drilled through with abundance of small holes. In the sunshine they look like a surface covered with golden nails, in another posture, like a surface covered with pyramids, in another with cones, and in other postures of quite other shapes, but that which exhibits the best, is the light collected on the object, by those means I have already described."

The *Micrographia* contains many biological observations, including among others spontaneous generation arising from the putrefaction of bodies, the nature of the vegetation of mould, mushrooms, sponges, &c. Hooke indicates how the stinging pain of nettle is created and discourses on the poisoning of darts. He gives a description of the shape, mechanism and use of the sting of a bee and demonstrates the contrivance and fabric of feathers for flying. He gives particulars of the parts and use of the head, feet and wings of a fly. He speaks of the generations of insects and discourses upon their actions. He analyses the fabric of the spider, making observations on the hunting spider. He describes a flea and a louse and gives tremendously enlarged drawings of them. Hooke

In this latter office he was principally responsible for rebuilding the City of London after the fire. In addition, he assisted Wren in the rebuilding of St. Paul's and many of the City churches. Hooke built the Monument, the home of the College of Physicians in Warwick Lane, Bedlam Hospital at Moorfields and many other important structures. Much more credit would have been given to Hooke to-day had he been able to have rebuilt London according to his own plan. The proprietors were in such a hurry to get their premises back and the expense involved in any complete rebuilding plan was so large for an impoverished exchequer, that it was only possible to rebuild on the old foundations. The same thing may easily happen after this war. Expediency may outweigh beauty of design and elaboration of plans in rebuilding London, and so we may find in the end the City looking much the same in the future as before the war. Much will have to be constructed on old foundations and old alignments.

Hooke was a tireless experimenter and the inventor of numerous valuable devices. He claimed over 100 inventions and it seems that his claim could be substantiated. Among his inventions were the anchor-escapement, which brought about a revolution in clock-making; his balance-spring, still found in our watches, which made possible the chronometer; his law of spring forms the basis for the theory of elasticity as employed by engineers, and his universal joint is an essential feature in transmission gear and for other purposes. He introduced freezing point as zero in the thermometer scale and made improvements in the microscope, the telescope and the air-pump. No wonder that John Aubrey, referring to Hooke, declared: "He is certainly the greatest mechanick this day in the World." In every branch of science then known, Hooke made important discoveries. The Royal Society expected him to produce experiments at each meeting and it was because he had to turn continually from one subject to another that he was never able to complete the investigation of any one vital subject. Questions were asked of him week by week and it hardly mattered what the subjects were, Hooke managed to give a more or less satisfactory answer. He was a man of keen intellect and although many of his replies were conjectures, they almost invariably turned out to be very near the truth. Many of his discoveries are of great value even to-day.

Although the variety of the experiments performed by Hooke was endless, there was always some practical object in view. Pepys mentions many discourses with Hooke and refers to them in his Diary. He doubted Hooke's claim to "tell how many strokes a fly makes with her wings" remarking that it was "a little too much refined". In another entry Pepys says: "This noon I met with Mr. Hooke and he tells me the dog which was filled with another dog's blood at the College the other day is very well and like to be so as ever, and doubts not its being found of great use to men." It will be remembered that, at that time, there was much discussion and experimentation regarding blood transfusion. Pepys also wrote that Hooke "is the least and promises the most of any man in the world that ever I saw". And Evelyn says: "I called at Durdans, where I found Dr. Wilkins, Sir William Petty and Mr. Hooke, contriving chariots, new rigging for ships, a wheel for one, to run races in and other mechanical inventions; perhaps three such persons together were not to be found elsewhere in Europe for parts and ingenuity."

Hooke eventually became a doctor of medicine, but he knew little of the cause and cure of disease. This was the case with many of the doctors of the seventeenth century. They did not realize that most of the minor ills and pains were caused by eating and drinking too much. At the least pain medicines were taken in quick succession and all kinds of remedies were tried. We have many instances of this in a Diary² which Hooke kept during the last thirty years of his life, parts of which have been published. Although these references to medicine are more amusing than instructive they do give an idea of the state of medicine in those days and emphasize the differences in opinion regarding diseases and cures.

Hooke had a weak stomach, but he made things worse by much eating and drinking which aggravated the trouble. Referring to himself on January 1, 1675, he says "eat meat and drank chocolate that rectified stomach and made me sleep well", and on the following day he wrote: "Could not sleep after chocolate till eating salt beef at 2 in the morning." Some days later he "Drunk claret which much disordered me, slept very little; after drinking ale, slept well". He further mentions that Madam Tillotson told him that "a souveraine remedy for the falling sickness was made out of the mosse of a man's skull" and that "Sir Christopher Wren told of killing the worms with burnt oyle" and "of curing his lady of a thrush by hanging a bag of live boglice about her neck". Mr. Wild told him "that the blood of a black cat would cure chilblains".

² *The Diary of Robert Hooke* (1935). Edited by H. W. Robinson and W. Adams, London.

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In the early days of the Royal Society the microscope played a great part in scientific discovery. So also did the air-pump, which was constructed for Robert Boyle by Hooke. He carried out experiments with the air-pump on animals, and plants, especially with regard to respiration and exhaustion. Hardly a meeting passed without Hooke being requested to prosecute his inquiries into biological subjects. His first experiments were made to describe the nature and quality of air. We read that on May 6, 1663, he was ordered "to bring in some experiments concerning the condensation of air, in order to make them in the compressing engine and explain: What animals will live in it, and what die? How those that live endure it? Whether pleasantly or with regret; if it seem painful to them and offensive? Whether it make them nimble and acute, or dull and sleepy?" The answer to these and to many other queries were given in papers published in the *Philosophical Transactions*. Hooke's work on respiration was, undoubtedly, of an elementary character, but we must remember that knowledge of this and other allied subjects was meagre in the seventeenth century. His experiments included many on animals to see how long they would keep alive in a closed chamber and how soon revive after blowing fresh air into their lungs. Waller remarks that this "plainly shows the use of air and the difference between venal and arterial blood". Hooke made a trial with a bladder, how long the same air would serve for respiration without the supply of fresh air; and he found that it served for five inspirations, though with difficulty. He later made an experiment of shutting up in an oblong glass a burning lamp and a chick; and the lamp went out within two minutes, the chick remaining alive and lively enough. He next tried the experiment of respiring the same air, both in a glass immersed in cold water, and in a bag. Mr. Balle respired in the glass 30 times, Dr. Merret 36, Mr. Hooke 13 and the operator 56. Then the same was tried in a bag, where Mr. Hooke respired 19 times in one minute and Dr. Merret 76 times in three minutes. When tried again, but this time with warm water, the operator respired 26 times in 1' 52" and Mr. Hooke 24 or 25 times in 1' 50".

On April 6, 1664, an account was given by Mr. Hooke of two birds, that were put, one into a glass with common air, closed with clay; the other into the compressing engine with common air likewise, but closed with cement. The bird in the glass, after it had been kept there eight hours, remained alive and pretty well; but the other bird closed up with cement, died within the same time. A few weeks later Mr. Hooke acquainted the Society with the success of the experiment made upon a dog cut open alive and kept so for above a whole hour, by means of a pair of bellows and a pipe thrust into the windpipe of the dog; whereby the lungs being blown, the heart continued beating for a long while after the thorax and belly had been displayed, and a great part of the diaphragm cut away. In a letter to Boyle, dated November 10, 1664, Hooke says: "The other experiment (which I shall hardly, I confess, make again, because it was cruel) was with a dog, which, by means of a pair of bellows, wherewith I filled his lungs, and suffered them to empty again, I was able to preserve alive as long as I could desire, after I had wholly opened the thorax, and cut off all the ribs, and opened the belly. Nay, I kept him alive above an hour after I had cut off the pericardium and the mediastinum, and had handled and turned his lungs and heart and all the other parts of its body, as I pleased. My design was to make some inquiries into the nature of respiration." After these few experiments on animals Hooke felt himself quite unable to face any further vivisections for we find that on later occasions, when asked to perform similar experiments, he excused himself and suggested that others should do the work. He continued to demonstrate his ideas regarding plants and the smaller animals but was inclined to devote most of his time after the first few years in London to problems concerning physics and mechanics, of which he was much more the master.

Robert Hooke died on March 3, 1703, and as a mark of respect all the Fellows of the Royal Society then in London attended his funeral. If his work in medicine and biology appears to us in these times to have been superficial and trivial it is perhaps because others who have benefited by his spade work have advanced his theories so that now they have become unrecognizable. The least we can do is to accord to him the credit that is due for having seen and understood many of the problems with which future generations have had to grapple and regret that time and opportunity did not allow him to follow up his own initial experiments.

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It is curious that one of the most interesting of Hooke's contributions to scientific thought, namely, his theory of combustion, should have sunk into comparative oblivion. Robison mentions the matter in his edition of Black's Lectures on Chemistry and speaking of Hooke's discovery of the role of oxygen in combustion says:

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Referring to this Robison says: "Can anything more be wanting to prove that this is the same with the modern theory of combustion? The eager mind of Hooke, attracted by every appearance of novelty, was satisfied with the general notion of a great subject, and immediately quitted it in chase of some other interesting object. Had he not been thus led off by a new pursuit, this wonderful man would not only have anticipated, but

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Referring to this Robison says: "Can anything more be wanting to prove that this is the same with the modern theory of combustion? The eager mind of Hooke, attracted by every appearance of novelty, was satisfied with the general notion of a great subject, and immediately quitted it in chase of some other interesting object. Had he not been thus led off by a new pursuit, this wonderful man would not only have anticipated, but

³ Antony van Leeuwenhoek and his "Little Animals," London, 1932.

to return to Michigan so that Beaumont, the "backwoods physiologist", as Osler called him, might continue the investigation. In 1833, Beaumont published his book *Experiments and Observations on the Gastric Juice and the Physiology of Digestion*. He wished to continue the work but Alexis was determined to return to his family. This time he was lost entirely for over ten years and when found, all efforts to secure his co-operation were unavailing. Beaumont died in 1853, and Alexis St. Martin lived for another twenty-eight years, dying at the age of 83. Sir William Osler attempted to secure a post-mortem, but the friends were adamant in their refusal. "Old fistulous Alexis" was truly elusive to the end.

The four series of experiments each lasted only a matter of months, yet the contribution to gastric physiology was of great value. The subject was rather an unwilling participant. Yet who can blame him? "Poor Martin," wrote Dr. McCall to Osler, "he is indebted to his stomach for his earthly immortality, as others are to their good deeds, and self-sacrifice".

Early subjects of ovariectomy.—Another American patient whose services to medical science deserve full recognition was Mrs. Jane Todd Crawford, upon whom Dr. Ephraim McDowell performed the first ovariectomy. Mrs. Crawford's service to medicine was a more heroic and praiseworthy performance than that of Alexis St. Martin. From her remote farmhouse in the wilds of Kentucky she came on horseback to McDowell's house in the town of Danville and there the operation was performed in December 1809. McDowell was assisted by his nephew and colleague James McDowell. "We removed fifteen pounds of gelatinous substance and then extracted the sac, which weighed seven pounds and a half." Five days later she was making her bed and in twenty-five days she returned home and lived for another thirty-two years. She died in 1841, in her 79th year. We know very little about Mrs. Crawford and we have no portrait of her. Neither doctor nor patient had any idea of the importance of the operation to posterity. Both are entitled to eternal gratitude, and Mrs. Crawford should share with Dr. Ephraim McDowell the honour due to the founder of ovariectomy.

The priority of the operation has been questioned and it has been claimed that the first ovariectomy was performed a century earlier, in 1701, by a Glasgow surgeon, Robert Houston. The patient was Margaret Millar, 38 years of age, who had an enormous ovarian tumour from which more than nine quarts of "glutinous substance" were removed at the operation. Whether the wall of the cyst was also removed is not clear from the description; it was nevertheless a bold operation. The wound was dressed with "compresses dipped in warm French brandy", and the patient made a good recovery and lived for thirteen more years in perfect health. That is all we know of Margaret Millar, but it is obvious that she was a woman of heroic fibre.

It is in the early part of the nineteenth century that one finds the most frequent mention of the names of patients in medical literature. Before that time they were seldom named unless they were persons of distinction; in more recent years it became customary to use initials, or merely to indicate age, sex and physique.

Pasteur and his patients.—Although he was a chemist and not a doctor, Louis Pasteur gave full credit to his patients for the part they played in the fight against rabies. The story of the Alsatian boy, Joseph Meister, aged 9 years, who was attacked by a mad dog and severely bitten as he was going alone to school on July 4, 1885, is well known. He was at once sent to Pasteur, who accommodated the mother and child in his laboratory and administered the inoculations which had hitherto been so successful on his dogs.

Pasteur was torn with fear and anxiety during the experiment; probably his worry was all the greater because he was not a medical man. Naturally he was more confident when, a few months later, he inoculated his second patient, a shepherd boy from the Jura, 14 years of age, named Jupille. This lad was in the company of a number of younger boys, when they were attacked by a large dog with foaming jaws. Jupille at once wrestled with the dog and succeeded in killing it, but not before he had been severely bitten. Like Meister he was accommodated and successfully treated in Pasteur's laboratory. His brave defence of his comrades is commemorated in a statue in the garden of the Pasteur Institute. Joseph Meister spent his life as a technical assistant in the Institute. He committed suicide when the Germans entered Paris.

The first child to be vaccinated.—Another patient whose name should be remembered was the first child to undergo vaccination at the hands of Edward Jenner. On May 14, 1796, Jenner inoculated James Phipps, a boy of eight years, with cowpox from the hand of a milkmaid Sarah Nealmes. Eight weeks later he inoculated the boy with smallpox, and no disease appeared. The proof was complete, but Jenner did not publish his dis-

[April 4, 1945]

The Patient: A Neglected Factor in the History of Medicine

By DOUGLAS GUTHRIE, M.D., F.R.C.S.Ed.

In his noteworthy Address, entitled *A Landmark in Modern Neurology*, delivered at the Royal Society of Medicine on November 27, 1934, to commemorate the fiftieth anniversary of Sir Rickman Godlee's pioneer operation for the removal of a cerebral tumour, Mr. Wilfred Trotter describes this important event in medical history, and tells us that "the young man's name was Henderson", and that "he was a native of Dumfries".

"One's professional mind, perhaps wisely, would prefer to conceal, under the comprehensive label of 'the case', the fact that this person was a human being, and would also prefer to limit any concession of individuality to such remarks as that he was of a good type and that he took the anæsthetic well. . . . "It is a strange defect in medical history to have kept so few of the names of these benefactors. . . . "Let us not forget, however, that they are the names of those who have borne more substantial witness than has yet been produced by any philosopher or any theologian that all suffering is not in vain."

In an effort to remedy this "strange defect in medical history" I wish to pay tribute to some patients of the past who have played an important part in the march of medical progress.

The earliest patients.—A study of the patient in medical history reveals some curious facts. In ancient times there appears to have been little professional secrecy. . . . The patient's name is mentioned in many of the descriptions of wonderful cures in the Greek temples of Æsculapius. Everyone who visits Epidaurus will see the stone of Hermodikes. Hermodikes was a paralytic who, during his sleep in the temple, was ordered by the god to go forth and bring in as large a stone as he could find. He brought the stone, which still lies in the Abaton, and he departed cured.

Hippocrates, though entirely free from this boastfulness, mentions the names of many patients: such as Philliscus, who lived by the wall, of whom we read that "his breathing was large and rare"—the first description of Cheyne-Stokes' respirations—and numerous others.

The patients of the Middle Ages and of Renaissance times are all forgotten, if indeed their names were ever recorded. Some of the case reports, such as those of Ambroise Paré, mention age and occupation, but not the name. Indeed it was not until the eighteenth and nineteenth centuries that it became usual to record the name of the patient in medical literature. Now, it has become merely initials or a number, and when honour is due it is like that accorded to the unknown soldier. Perhaps George Eliot was thinking of this as she wrote the last chapter of "Middlemarch" and noted that "the fact that things are not so bad with you and me as they might have been is half owing to those who led hidden lives and rest in unvisited tombs".

Of course the contribution of the patient is passive, and few patients, even if they happen to be also medical men, are concerned with the benefit to humanity which may accrue from their sufferings. Nevertheless, even if some patients have had their greatness thrust upon them in such unpleasant fashion, they are none the less worthy to be remembered, and it is unfortunate that so many of them are unknown and that even their names are unrecorded. It is therefore all the more necessary to preserve such scanty records as we possess of the patients who have contributed to the progress of medicine.

William Beaumont and Alexis St. Martin.—Probably the most familiar of all is Beaumont's celebrated patient, Alexis Semata or St. Martin, "the man with no lid to his stomach". It is unnecessary to repeat the familiar story—the accident on June 6, 1822, when the young trapper of 19 years was shot in the abdomen at close range—the unexpected survival and ultimate recovery with a gastric fistula—Beaumont's resolve to view through this window the process of digestion, as yet ill understood—his efforts to keep his elusive patient under observation and to convince the Army authorities of the value of the investigation—all this forms a well-known story, one of the most romantic in medical history. Beaumont's observations were by no means continuous, for scarcely had he embarked on his scheme of research, in 1825, when his patient, whom he had fed and clothed and housed at his own expense, suddenly disappeared and was lost to view for two years. Then he was discovered in Canada, 1,500 miles away, where he was now married and had two children. Two more years elapsed before Alexis could be persuaded

Naturally, a disease or an instrument associated with a distinguished patient attracts popular attention. Nélaton's invention, the porcelain-tipped bullet probe, was first used to locate a bullet in the arm of Garibaldi. The fatal illness of the Emperor Frederick, during which Sir Morell Mackenzie was so severely criticized, drew attention to cancer of the larynx and advanced our knowledge of the subject. The operation for appendicitis upon King Edward VII focused attention upon the disease, to the great benefit of many less illustrious patients.

Post-mortem services.—Sometimes the patient confers a benefit upon humanity only after his death. Although, naturally enough, it is unusual for a pathologist to publish the name of every patient from whom a given specimen has been obtained, there are a number of "classic" pathological specimens and the names of some of their original owners are known. Such is the well-known kidney of John King, a sailor aged 34, who was treated at Guy's Hospital in 1825 by Richard Bright. From a study of this case Bright concluded that dropsy might be due to kidney disease and he thus greatly advanced the study of nephritis. Bright's *Reports of Medical Cases* are models of clear reporting and logical reasoning.

It is said that the specimen which illustrates emphysema in Matthew Baillie's *Morbid Anatomy* is the lung of Samuel Johnson. There have been many instances of patients who have desired a post-mortem examination in the hope that others might receive benefit. Such was Sir James Mackenzie who died of angina pectoris and whose coronary arteries were found to be greatly thickened and calcified.

The gruesome interest of those post-mortem records is apt to be a little repellent when applied to distinguished persons who, like Sir Thomas Browne, have been "knaved out of their graves after many years" and subjected to scientific scrutiny. One of the most recent investigations concerns the mummified remains of Francisco Pizarro, described in detail in 1941. "Who knows the fate of his bones?"

The doctor as patient.—Another interesting aspect of the contribution of the patient to medical progress is revealed by a study of the doctor who is himself a patient. There have always been medical men who did not hesitate to experiment upon themselves in the interests of science; men like John Hunter, who shortened his life by an unfortunate effort to investigate the cause of syphilis, or like Henry Head, who had his radial nerve divided in order that he might study its regeneration, or Sir J. Y. Simpson who spent hours with his friends Thomas Keith and Matthew Duncan inhaling various vapours until they discovered chloroform.

Many an investigator has become the victim of the disease he sought to elucidate, notably in the field of tropical medicine. Lazear, Adrian Stokes and Noguchi died of yellow fever; Ricketts of typhus, Dutton of trypanosomiasis; and there have been many other martyrs to science.

The largest class of all doctor-patients includes those medical men who, from no wish of their own, nor even by direct infection, have been smitten by disease but who have turned the experience to good account. In 1683 Sydenham gave a graphic description of gout, based upon his own personal experience. Laënnec died of tuberculosis, which he had done so much to elucidate. Bostock in 1819 gave the first clear account of hay fever and described his own case. Thomson, in 1876, described the disease associated with his name (myotonia congenita or Thomson's disease), which was hereditary in his family; and Nothnagel, who died of angina pectoris in 1905, recorded his sensations up to the very moment of his death.

In more recent times Sir Frederick Banting related that the first patient to be treated by insulin, in 1922, was Dr. Joe Gilchrist. Gilchrist had diagnosed his own diabetes in 1916 but his sugar tolerance did not break down until 1921. He was the subject of many of the early experiments with insulin and his medical training enabled him to contribute valuable information regarding the subjective aspects of insulin.

One of the best descriptions of a disease by a medical man who suffered from it is given in Dr. Leonard Mark's *Acromegaly, a Personal Experience*, which appeared in 1912. "I was walking across Cavendish Square one afternoon in November 1905, when the idea suddenly seized hold of my mind that I might be suffering from acromegaly, which would account for my headache and enlargement of hands and feet." Then he discovered that his friends had long since diagnosed his complaint but had decided not to tell him. Dr. Mark was then 50 years of age. He died in 1930 at the age of 75. His careful record of his own symptoms was a valuable addition to our knowledge of acromegaly.

Even more dramatic, though written as a popular rather than as a scientific work, is an account by Dr. Puder, of three operations for appendicitis, entitled *On the Danger List*

covery until two years later when he described 23 successful cases in his "Inquiry into the causes and effects of variolæ vaccinæ". Although this was the first vaccination with cowpox, Jenner had experimented on his own baby son, Edward, seven years previously, inoculating him with swinepox which he believed to be similar to smallpox. But long before that date the cowpox tradition was well known in Gloucestershire, and a cattle dealer named Benjamin Jesty, in 1774, inoculated with cowpox his wife and his two sons. In 1805 he visited the Jennerian Institute in London and substantiated his claim to have been the first vaccinator. His wife, the first to be intentionally vaccinated, lived to the age of 84. Thus once again did the patient contribute to the advance of medicine.

Patients under anæsthesia.—In another discovery, that of anæsthesia, the patient played an essential part and the names of most of the pioneers have been recorded. In 1842, Dr. Crawford Long, of Jefferson, Georgia, administered ether to a lad of 19 named James Venable and removed a sebaceous cyst from his neck, but this important discovery was not published, and remained unnoticed for years. Venable was a friend of Dr. Long, as well as his patient; indeed, the two had participated in "ether frolics", in which the stimulant effect of ether inhalation was exploited as a fashionable amusement. Long wrote: "I mentioned to Venable the fact of my receiving bruises without suffering, when under the influence of ether and I suggested to him that the operation might be performed without pain. It was done on March 30, 1842, and Venable did not experience the slightest pain." He was a brave man, and he deserves to share in the honour due to Crawford Long.

In 1844 Horace Wells, a dental surgeon, persuaded Gardner Colton, a travelling lecturer in chemistry, to give him nitrous oxide to inhale, while a colleague extracted a tooth. In October 1846 William T. Morton, after having, by the use of ether, painlessly extracted a tooth from a patient named Eben Frost, persuaded a surgeon, John Collins Warren, to allow him to anæsthetize Gilbert Abbott, a man aged 20, who was to have a tumour removed from the neck. "Are you afraid?" asked Morton. "No," was the brave answer, "I am confident and will do precisely as you tell me." Truly the ideal patient. The news of ether soon reached England and Robert Liston was the first to try it at University College Hospital in December 1846. The patient's name was Frederick Churchill, a butler aged 50, and he had a malignant growth of the leg, which demanded amputation through the thigh. Peter Squire administered the anæsthetic, and Liston completed the operation in thirty-two seconds. When the patient recovered consciousness he did not know the operation was over but on seeing the uplifted stump he burst into tears. The scene in the theatre was most impressive and tense. But was the patient the first subject of ether anæsthesia in Britain? Apparently not, according to Sir Charles Brown, of Preston, who was a spectator of Liston's amputation and who describes it in "Sixty-four years a doctor" (1922). "Before the patient was brought in", he wrote, "the anæsthetist asked the students for some volunteer who would submit to be anæsthetized. A young man named Shelbrake, of powerful build and a good boxer, at once came forward and lay on the table. After he had inhaled ether for half a minute he suddenly sprang up, felled the anæsthetist at a blow and scattered the students before him like sheep before a dog. He soon regained his senses and then the patient was brought in."

THE DISCOVERY OF ANÆSTHESIA

Date	Anæsthetist	Surgeon	Patient	Anæsthetic	Comment
1824	H. Hickman	(Experiments on animals)	(animals)	Nitrous oxide	
1842	C. W. Long	Long	Jas. Venable	Ether	
1844	G. Colton	—, Riggs	Horace Wells (tooth)	Nitrous oxide	"A new era in tooth pulling"
1846	W. T. Morton	Morton	Eben Frost (tooth)	Ether	
1846 Oct.	W. T. Morton	J. C. Warren	Gilbert Abbott	Ether	"Gentlemen this is no humbug"
1846 Dec.	P. Squire	R. Liston	Frederick Churchill	Ether	"This Yankee dodge beats mesmerism hollow"
1847	J. Y. Simpson	J. Miller	"A Highland boy"	Chloroform	

The first subjects in other discoveries.—It is a pity that we do not know the name of the first patient to experience the benefits of Lister's discovery. All we know is that he was "James G—, aged 11 years, admitted to Glasgow Royal Infirmary on August 12, 1865, suffering from compound fracture of the left leg caused by the wheel of a cart passing over the limb". Splints and a carbolic dressing were applied and the wound and fracture healed uneventfully. One of Lister's minor inventions, that of the rubber drainage tube, was first used to drain an axillary abscess, the patient being Queen Victoria. Dr. John Snow gave chloroform and Sir William Jenner worked the carbolic spray.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[March 15, 1945]

The Paget Cell: Its Structure, Occurrence and Significance

By Professor E. MEIROWSKY, M.D., and S. KEYS, L.R.C.P., M.R.C.S.
(Technical Assistance by P. H. Jacobs and Hyla M. Holden)

THE object of this paper is to give some further details as to the structure, occurrence and significance of the Paget cell.

The structure of the Paget cell.—As early as 1921 one of us (E. M.) described and illustrated in the cells of a squamous-cell cancer, chalk-white, translucent and plastic bodies, which were either spherical, oval, or pear-shaped. They did not take up the usual stains and carried with them a layer of chromatin. These bodies were surrounded by a very fine outline (figs. 1—6) and appeared to be exceedingly malleable and of a viscous consistency. These features could be easily recognized when the diaphragm of the microscope was almost closed and a green filter introduced, or by examining the sections with a binocular microscope.

Several pathologists, biologists and dermatologists, amongst them P. G. Unna, were shown these findings and they unanimously declared that they had never recognized them before, although it soon became clear that they represented nothing else but the so-called Paget cell in a squamous-cell cancer. Hints of their occurrence can be found in earlier literature, e.g. H. Leloir (1878) and J. Renaut (1881) speak of "globules blancs", which they consider to be connected either with the nucleus of the epithelial cell or formed by migrating cells.

During the course of experiments on psoriasis we observed the same phenomenon in a rabbit's cornea, which had been inoculated with an extract of another cornea, previously injected with psoriasis material. Only one difference was observed, viz. the bodies in the rabbit's cornea contained in their interior a marked trabecular structure and tiny dots. For this reason we went back to Meirowsky's findings, studied again the Paget cell and compared it with the cells of tar cancer and with the so-called vacuolated cells of carcinomatous ascites and pleural fluid.

Figs. 1 to 6 show the spherical bodies with their fine outline extruding from the nucleus of the cells of a squamous-cell cancer. Their pellicle is translucent; this is proved by the fact that the posterior wall of the cavity in which they are lying becomes blurred (figs. 1 and 2). This apparent shadow, however, becomes distinct when brought into focus. Any doubt can be set at rest by dark ground illumination of fresh preparations in which the bodies can be seen to be plastic and can be compared to soap bubbles. Their fine, thin outline is sharply differentiated against the surroundings. This description applies also to Paget cell (figs. 13, 18, 23), to the cells of carcinomatous ascites fluid (fig. 24) and to many cells of tar cancer not pictured in this table.

(1938). The first two operations were for the drainage of an abscess, the third for removal of the appendix, and the anæsthetics were local, general and spinal anæsthesia. Whether we approve the publication of this case history for popular reading or not, we must admit that it is an excellent statement of the patient's point of view. Another work of this nature is *A Journey Round My Skull* (1939) by S. Karinthy, a sufferer from a cerebral tumour who ultimately died of his disease some time after the book was published. Both writers appear to have been of Hungarian nationality and it would seem as though this form of literature has a special appeal on the Continent. In Britain it is regarded as proof of a somewhat morbid taste and although many of us revel in murder mysteries we usually prefer fiction to fact.

Self-treatment by patients.—The patient who suggests methods of treatment to his doctor is not always popular and is apt to be a nuisance. Nevertheless there have been ingenious persons who have materially contributed to their own cure by suggesting ways and means. A good example was Isambard Brunel, the distinguished engineer who designed Clifton Suspension Bridge, the *Great Eastern* steamship, and other notable works. In 1843 Brunel was amusing some children by pretending to pass a half-sovereign from his ear into his mouth, when he inadvertently inhaled the coin. An attack of choking was followed by persistent coughing and the patient could feel the coin move in his windpipe when he coughed or bent forward. Sir Benjamin Brodie attempted to remove it through a tracheotomy wound but failed on several occasions, and at last, six weeks after the accident, Brunel had a table constructed which could be moved into a vertical position. To this he was strapped, then inverted and shaken, and after a few coughs he heard what he called the delightful music of the coin clinking against his teeth. The affair created quite a stir, as Brunel was a figure of national importance.

In the category of self-experiment may be placed Manuel Garcia, the singing master who was curious to see his own vocal cords and who invented the laryngoscope in 1854, although he had no idea then that he was founding a new medical specialty. He lived to the age of 101 and thus reaped the honour which was due to him.

The dangerous patient.—All the patients whose names have been mentioned made a beneficial contribution to medicine. Nevertheless there have been others whose influence has been of negative character. Probably the best example is the typhoid carrier Mary Mallon; "Typhoid Mary", as she was called. This unfortunate woman was a cook to various wealthy families in and around New York and she flitted from one situation to another after the fashion of cooks, producing one typhoid epidemic after another until at last, in 1907, the cause was revealed. The Department of Health felt bound to take action, but Mary refused to co-operate and when force became necessary she fought vigorously with the four policemen who had been sent to bring her to hospital. For three years she was kept under supervision. Then she was released after promising to give up her vocation of cook and to report at regular intervals. Unfortunately she broke her promise, changing her name and working as a cook in hotels and restaurants. Eventually, while employed as cook in a hospital in which typhoid had appeared, she was identified, and once more she was isolated, this time without resistance. She was given employment in the laboratory of the isolation hospital and there she remained until her death in 1938. She had been the direct cause of 53 cases of typhoid and probably of other cases which were never traced. The lot of the carrier is indeed unfortunate, deserving of all the sympathy and help we can give.

CONCLUSION

This theme of the patient as a factor in medical history might be enlarged but perhaps enough has been said to indicate the importance of a neglected topic. I have ventured into the subject for three reasons:

First, because so many of the patients associated with medical progress are apt to be forgotten, though they are worthy to be remembered and honoured.

Secondly, because so much attention is now devoted to the chemistry and physics of organs and tissues and excretions that the man himself is obscured.

Thirdly, because we need to be reminded that the doctor has much to learn from the intelligent patient.

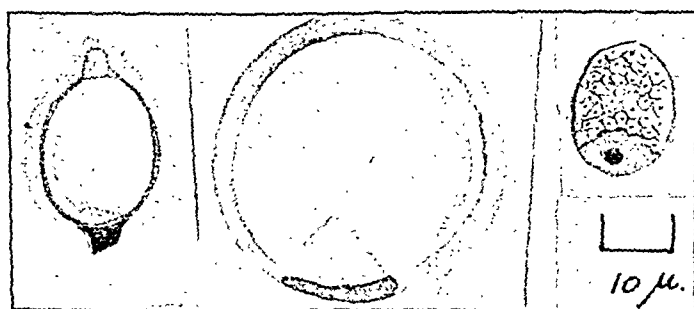
length, 40 microns in width and 12 microns in depth (fig. 24). The second group deals with the inner structure of the large spherical bodies as shown in figs. 18, 23, 24, 29. Careful focusing into the depth of the cell often reveals a marked trabecular structure, which contains tiny dots between the strands of the trabeculum (figs. 19, 25, 30 to 33). The last group of spherical bodies shows a striking feature, viz. a kind of budding. This phenomenon is not a new observation but has already been described by R. J. Ludford and G. M. Findlay (1926) in the virus vacuoles of fowlpox. The process commences with the formation of a fine pattern of lines on the surface of the spherical bodies (fig. 20), and progresses by deeper stained lines which cut through the spherical bodies and divide them into two, three or even more balls (figs. 21 and 22). By focusing carefully with the micrometer screw, one can clearly see the membrane, which forms in this way and separates the spherical bodies.

The nucleus is also involved in this process. It does not become pyknotic, its nucleoli stain well and remain unchanged, but it is often cast off to the edge of the cells as a small, round or half-moon-shaped body, imitating in this way the well-known features of a molluscum contagiosum body. (Figs. 13, 15, 18, 19, 20, 21, 23, 25, 31 to 33.)

There is still another feature of the Paget cell to which reference should be made and which has already been reported by J. Darier (1920) as "cellules à manteaux" and by J. M. H. MacLeod and I. Muende (1940), namely the appearance of a double contoured



Girdle cells. 26 P. $\times 2000$.



23 P.

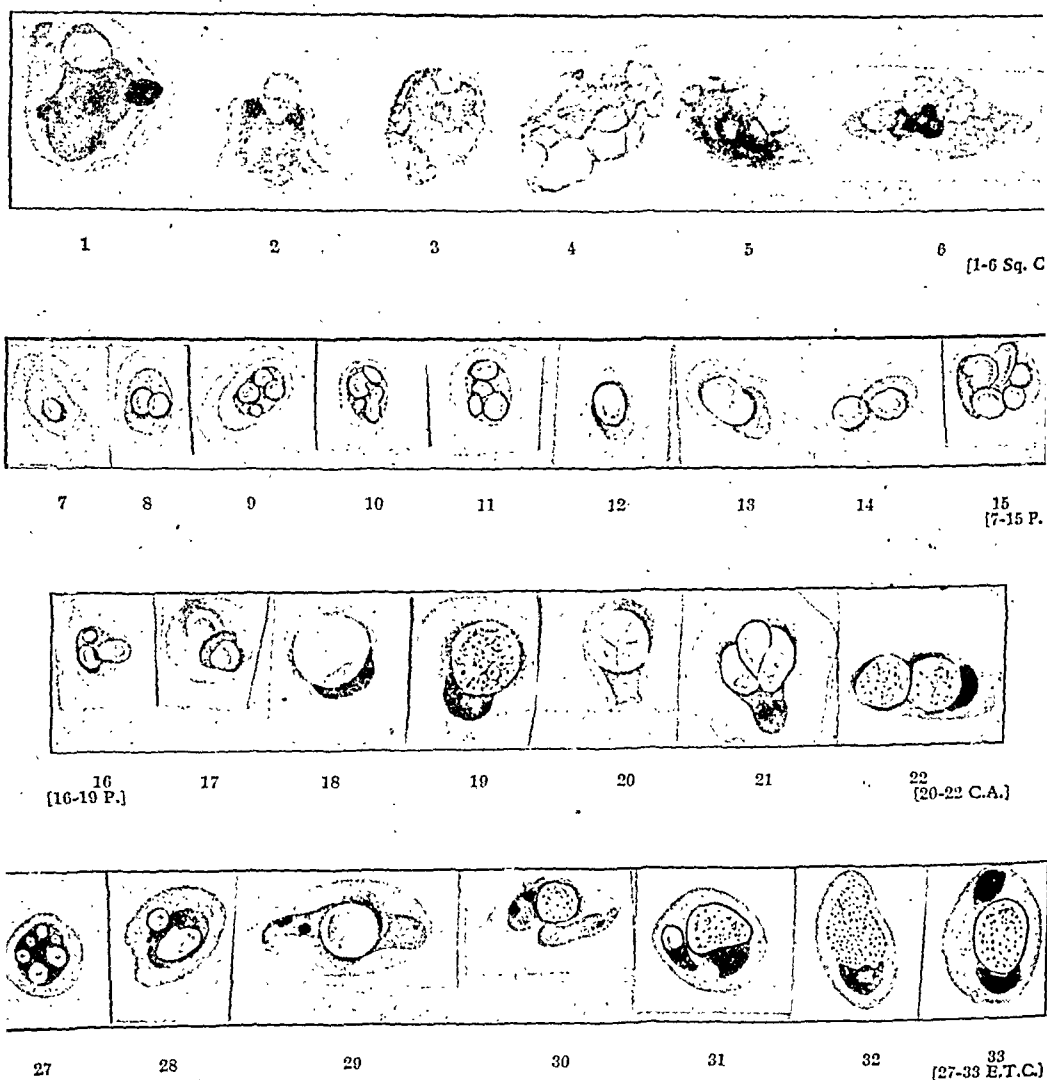
24 C.A.

25 P.

coat round the cell. We have found such cells not only in Paget's disease but more often in carcinomatous ascites and pleural fluid and in different cancers, especially after fixation with osmic acid vapours.

If a vacuole is defined as a cavity containing air, fluid or solid substances, then our findings are not consistent with the definition of a vacuole. We found spherical bodies surrounded by a fine pellicle and often showing marked trabecular structure and tiny dots between the strands of the trabeculum.

The findings in all three diseases can be divided into three groups: The first deals with the appearance of the spherical bodies within the nucleus and protoplasm (figs. 7 to 33). Within the nucleus (figs. 7 and 8) one or two separate balls can be seen, approximately 2 microns in diameter. Such intranuclear inclusions have been observed by several authors and references can be found in F. Fischmann's and D. Russell's paper on intranuclear inclusions in cultures of fetal leptomeninges (1940). They increase in number and size (figs. 9 to 11, 27) and coalesce until the entire nucleus is filled by a kind of blister (fig. 12), which is eventually extruded from the nucleus (figs. 13 to 16).



Sq. C.—Squamous cell cancer.
P.—Paget's cell.
C.A.—Carcinomatous ascites fluid.

E.T.C.—Experimental tar cancer.
[All figs. $\times 060$ except fig. 26.]

Frequently those spherical bodies are extruded from both ends of the nucleus, which encircles them like a girdle (girdle cell, figs. 17 and 26). The spherical bodies in the cytoplasm lie as separate balls, compressing the half-moon shaped nucleus to the border of the cell (fig. 15). When they coalesce they form a single large spherical body (figs. 18, 23, 24, 29). Paget cell fig. 23 is 22 microns long, 17 microns wide and 6 microns deep. The spherical bodies in carcinomatous ascites fluid develop to a size of 40 microns in

An outstanding feature is the affinity of the dots to osmic acid compounds. However, according to Lison (1933), osmic acid is not a reagent that identifies even fatty substances in general and it has no histochemical value whatever. It is unlikely that the dots are of a fatty character since they are not dissolved by xylol. It is possible that they consist of lipid-protein, but confirmation is still lacking.

As the nature of the dots cannot be made out, we suggest that they should be called X-dots until further information about their nature is forthcoming.

There remains the possibility that the spherical bodies and the X-dots might be products of degeneration or fixation, but degeneration cannot play any part in their formation, since X-dots have been observed in mitoses and both spherical bodies and X-dots have been seen in basal cells and in normal tissues of the rabbit and man. The demonstration of spherical bodies and X-dots by vital staining with neutral red or 1% toluidin-blue alcohol (Scott's technique, Lee's *Microtome*, para. 761) and dark ground illumination, and F. Himmelweit's findings of "extrusion bodies" in the living allantoic membrane infected with ectromelia or vaccinia is at least strong circumstantial evidence against the conception that they could be caused by fixation.

The significance of the Paget cell.—As a result of close observation we conclude that the Paget cell develops from the normal epithelial cell. It has the same structure as the so-called vacuolated cells of carcinomatous ascites and pleural fluid and the cells of tar cancer. The changes which characterize the Paget cell are not the product of degeneration or of fixation, or a peculiar type of intracellular cedema or a disturbance of glycogen metabolism or vacuoles. The Paget cell is not a misplaced embryonal germ cell or a nevus cell or a melanoblast. Whether the Paget cell is according to L. Savatard (1935) and other authors already a cancer cell is a question which cannot be answered satisfactorily as cells of the type of Paget cells are not specific for Paget's disease only. We conclude, therefore, that the process occurring in the Paget cell is a normal response of the epithelial cell towards different kinds of animate and inanimate stimuli among which are tar, X-rays, sunlight, viruses and the unknown causes of cancerous conditions, psoriasis and lichen planus.

We are fully aware that the Paget cell needs further investigation by modern methods such as ultraviolet light, fluorescence and electron microscopy which were not available to us.

ACKNOWLEDGMENTS

One of us (E. M.) would like to express his sincere gratitude and indebtedness to Dr. J. Ferguson, County Medical Officer, Surrey County Council, and to Dr. R. C. Matson. We are both grateful for the help given us by the Medical Staff of Royal Surrey County Hospital, Guildford; to Professor A. Loewenstein (Glasgow), who introduced us to ophthalmological technique and took great interest in our problems; to Colonel W. F. Harvey (Edinburgh); to Professor W. E. Gye and Dr. B. D. Pullinger (Cancer Research Fund) and to Dr. H. J. Wallace (Woking) for valuable material; also to Mrs. Evelyn Merrow, who spent much time in helping us with the drawings.

Illustrations.—Figs. 1 to 6 from E. Meirowsky's paper (1921). Half-schematic drawings (figs. 7 to 25, 27 to 33) by Mrs. Evelyn Merrow. Paget's disease figs. 7 to 19, 23, 25, carcinomatous ascites fluid 20 to 22, 24, experimental tar cancer figs. 27 to 33. Photomicrograph of Paget's disease (fig. 26) by Mr. Eric O. Sonntag. The description of above is given in the text.

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Occurrence of Paget cells.

The occurrence of Paget cells is not limited to Paget's disease. They are found in many virus diseases and it is not surprising that research workers on virus diseases no longer speak of "virus vacuoles" but of "virus bodies" (C. E. Woodruff and E. W. Goodpasture, 1929); "virus blisters" (K. Herzberg, 1936); and even "extrusion bodies" (F. Himmelweit, 1938). These are all analogous to our findings, pictured in this paper. Such cells are further found in sarcoma, trachoma, psoriasis, lichen planus, pemphigus, Bowen's disease, non-gonorrhoeal endometritis. Even in normal skin (prepuce) and in embryonic skin of calves spherical bodies can be easily demonstrated, but the presence of the dots seems to be a very rare occurrence. Up till now, the spherical bodies have not been demonstrated in mitoses, but the dots are present in almost 90% of all mitoses in tar cancer, Shope's virus papilloma, Paget's and Bowen's disease. There are none in normal rabbit's testicle and very few in normal skin. Spherical bodies play furthermore a considerable part in the formation of melanin; this we have studied in the shaved skin of normal rabbits, exposed to sunlight. This occurrence has already been illustrated in E. Meirowsky's monograph "On the Origin of Pigment of Melanin in Skin and Eye" (1908), but its true nature was not recognized at that time. They further occur in the development of normal melanoblasts and goblet cells. They could be produced experimentally in the rabbit's cornea by different methods, and spherical bodies with dots developed after a first passage of material obtained from a cornea, previously injected with psoriasis serum, into a normal rabbit's cornea.

STAINING AND CHEMICAL PROPERTIES OF SPHERICAL BODIES AND DOTS

Beside the routine staining with hæmatoxylin-eosin, Pappenheim-Unna, Giemsa, methylene-blue, safranin, neutral red and osmic acid, we have used a method worked out by P. H. Jacobs, which stains the nucleus blue, the nucleolus bright red, the trabecular structure and the dots deep blue. The procedure is as follows:

(1) Fix tissues in Bouin or sublimate alcohol. (2) (a) After Bouin fixation treat sections for two minutes with 5% sodium thiosulphate solution. (b) After sublimate fixation treat sections for one minute with 0.5% iodine in 70% alcohol followed by "hypo" solution for two minutes. (3) Stain sections with carbol fuchsin, two to five minutes (basic fuchsin 1 gramme, absolute alcohol 10 c.c., 5% phenol in aqua dest. 100 c.c.). (4) Wash off excess stain in running water. (5) Differentiate in 96% alcohol till nuclei stand out bright red. Control with microscope. (6) Wash and mordant with 10% aqueous tannic acid for 1 minute. (7) Wash well and stain with 0.5% aqueous toluidin blue for one to two minutes. (8) Wash and dehydrate rapidly with absolute alcohol to which have been added a few drops of glacial acetic acid (optional). (9) Clear in xylol and mount in balsam. To get satisfactory results, it is essential to differentiate properly, since it is difficult to balance between blue and red shades.

The spherical bodies cannot be stained even by neutral red, which is the usual stain for vacuoles (Bolles Lee's "The Microtome and Vademecum", Par. 766, 1937). They are not blackened by osmic acid like the virus bodies of fowlpox (R. J. Ludford and G. M. Findlay, 1926). Sometimes the underlying nucleus is stained so deeply that the optical phenomenon caused by the transparency of the balls gives the impression that the balls are stained. Several authors have claimed to have succeeded in staining the "vacuoles" of molluscum contagiosum, but it is probable that they have stained the mucoid, jelly-like matrix (Goodpasture and Woodruff, 1931; Van Rooyen, 1938) in which the elementary bodies are imbedded. The pellicle of the spherical bodies does not give the iodine reaction for glycogen, as do the bodies of molluscum contagiosum (C. E. van Rooyen, 1939). It is impossible to break them up by trituration or to isolate them by trypsin digestion, as one can with the bodies of fowlpox (E. W. Goodpasture and C. E. Woodruff, 1931). They have no relationship to Unna's balloon degeneration with its 2 to 32 nuclei, or to H. Leloir's (1878) alteration cavitaire with its deposit of fibrin and formation of a loculated blister, when several adjacent cells undergo the same degeneration. Our cells are found amongst normal cells and do not develop into blisters. The possibility of our spherical bodies being the forerunners of H. Leloir's alteration cavitaire (1878) cannot, however, be ruled out but must be decided upon by further research on this special subject.

The dots can be stained by acid and basic stains. They are amphophilic like the elementary bodies of molluscum contagiosum. They might be chromatin substances or nucleolar extrusions or viruses. The positive Feulgen test is looked upon as the most reliable test for chromatin and viruses are considered to be Feulgen negative. The Feulgen reaction depends on the Schiff reaction for aldehydes and is given by the desoxy- and not by the ribose sugars. Consequently it does not show up chromatin containing the latter, even after a prolonged hydrolysis, which Bourne (1942) suggested for the demonstration of chromatin containing ribose sugars. Although according to this test our dots do not appear to be chromatin, this possibility cannot be ruled out since a negative Feulgen reaction does not exclude chromatin (Torbjörn Caspersson, 1936). For this reason a negative Feulgen reaction cannot be looked upon as a reliable test for viruses.

In regarding nucleolar extrusions as possible forerunners of the dots, we have found that they never give the staining reactions of the nucleoli by Jacob's method, but also here it must be remembered that the staining reactions depend on the fixation. As, according to R. J. Ludford (1921), the nucleolus is composed of a basophil and an oxyphil part, it seems not impossible that slight changes of pH could also reverse the staining properties of the dots.

similar attack in July 1944. Attributes condition to sensitivity to wool. In addition, has had urticaria since December 1944. For a number of years he has had indigestion and intolerance to fatty foods. Has had occasional pain in right upper quadrant which radiated to back, but was not colicky in nature. Has never been jaundiced. He has had kidney stones.

On examination.—Other than marked adiposity and occasional tenderness to palpation in right upper quadrant of abdomen, physical examination is negative with the exception of the skin.

Skin (December 1, 1944): Numerous excoriations over legs, abdomen and back. In addition, there were slightly raised, yellowish-tan, oval papules over the trunk, a few of which had a saffron-yellow colour. They were soft and only slightly raised and erythematous. They did not urticate when rubbed. Examination to-day shows the lesions clearly, but they are not as papular nor as yellow, but are pigmented. This consists of a peculiar yellowish-tan discoloration rather than of a true melanosis. The lesions have a pityriasis rosea distribution and are best seen on the left side of the chest and abdomen.

Course.—The interesting feature has been the change in appearance of the lesions from day to day. Within forty-eight hours after his first admission the papular element practically disappeared as well as several of the yellowish papules, leaving residual tannish-yellow macules. As the lesions disappeared, the cholesterol content of the blood dropped.

Laboratory data.—Blood-count, urinalysis, glucose tolerance, hippuric acid tests are all negative or within normal limits. X-rays of skull, K U B, sinuses, gall-bladder and I.V. urogram negative. Basal metabolic rate—plus 1. Icteric index 8 mg./100 c.c.

BLOOD LIPIDS

	Normal	Patient
Cholesterol	140-180 mg./100 c.c. plasma	400 mg./100 c.c. (4.12.44)
Cholesterol	140-180 mg./100 c.c. plasma	280 mg./100 c.c. (18.12.44)
Cholesterol esters	110-145 mg./100 c.c. plasma	250 mg./100 c.c. (18.12.44)
Total lipids	600-1,000 mg./100 c.c. plasma	1,496 mg./100 c.c. (18.12.44)
Lecithin	175-330 mg./100 c.c. plasma	Test unsatisfactory (18.12.44)
Cholesterol	348 mg./100 c.c. (26.12.44)
Cholesterol	430 mg./100 c.c. (28.12.44)
Cholesterol esters	270 mg./100 c.c. (28.12.44)
Cephalin	290 mg./100 c.c. (28.12.44)
Lecithin	493 mg./100 c.c. (28.12.44)
Total lipids	1,744 mg./100 c.c. (28.12.44)
Lipid phosphorus	12 to 14 mg./100 c.c. whole blood	19.7 mg./100 c.c. (28.12.44)
Cholesterol	380 mg./100 c.c. (9.3.45)

Biopsy: Paraffin section: H. and E. stained. Some perivascular infiltrate, particularly in the papillary body. No xanthoma cells seen.

Frozen section: Stained for fat with Sudan. Capillary vessels in the papillary body thickly studded with fat droplets. Some diffuse fat staining of the connective tissue.

I am indebted to my chief, Colonel Pillsbury, for the privilege of presenting this case and to Dr. Freudenthal for his assistance in preparing the histological sections.

This case has been shown for three reasons: First to ask your help in making a diagnosis as to the type of cutaneous lipoidosis with which we are dealing; secondly, to illustrate the sometimes apparent insignificance of cutaneous expressions of systemic disorders, and thirdly, to show the value of certain laboratory investigations.

When this man was first seen he did present slightly more obvious lesions than he does now, but at no time were they pronounced. At first residual pigmentation from neurotic excoriations or insect bites was considered, but the peculiar yellowish discoloration suggested that the patient might have a cutaneous lipoidosis, of a type we had not seen before, and hence we attempted to investigate it accordingly.

We have searched the literature rather carefully and have been unable to fit this case into any recognized classification. The usual types of xanthoma can easily be excluded, whereas some of the rarer lipoidoses, such as extracellular cholesterosis, necrobiosis lipoidica diabetorum, lipoid proteinosis and others, can also be eliminated both on clinical and histological findings. This case has some of the characteristics of the entity, xanthoma eruptivum, popularized, though not originally described, by Thannhauser and Magendantz (1938). The lesions are papular, pruritic, and change their appearance frequently. At times they are quite noticeable, whereas on other occasions, such as now, they are involuting. Once, as the cholesterol content of the blood dropped the lesions became much less manifest. Also in favour of xanthoma eruptivum is the marked elevation of blood lipids—especially the cholesterol content, and the presence of

Psoriasis and Alopecia.—ALICE CARLETON, M.D.

The patient is a married woman, aged 31. She gives a history of recurrent alopecia areata since the age of 15. There is a family history of alopecia on both sides. About two years ago she developed patchy psoriasis of the scalp, with a few scattered patches on the limbs. With the onset of pregnancy, the hair fell out over most of the scalp, and when it came back after the birth of her child, it grew first on the psoriatic patches, and about a month later on the non-scaly areas. A few months later, the hair fell again, and on this occasion, the patches affected with psoriasis were almost entirely spared, and the loss was almost exclusively confined to the non-psoriatic areas.

This suggests that the vascularity of the psoriatic areas acts as a bar to the appearance of alopecia areata, or, if the alopecia does occur, the vascularity accelerates regrowth. This in turn leads one to think that the origin of alopecia areata may be a vasoconstriction of small cutaneous fields, due perhaps to a toxin with a selective effect on sympathetic terminals in this position, comparable to the selective effect of thallium acetate on certain sympathetic endings while others are spared.

Lichen Nitidus.—Captain J. ROBERTS, R.C.A.M.C., for Major N. M. WRONG, R.C.A.M.C.

The patient is a 25-year old Canadian soldier who first noticed an eruption on his left ankle about a year ago. During the next five or six months other areas of the skin became affected. He now shows lesions on the right antecubital fossa, both forearms, right hip, glans penis, and shaft of the penis, and on the buccal mucosa.

Cases of lichen nitidus have been presented to the Section before by Dr. Barber, Dr. Dowling and others. The aetiology is essentially unknown; there is a suggestion that the eruption is of tuberculous origin; Dr. Barber has pointed out that in the original cases described in Germany by Pinkus, all the patients had venereal disease. This patient has had gonorrhoea but one would hardly expect that there was any relation between gonorrhoea and lichen nitidus, otherwise there would certainly be more cases of this condition in the Armed Forces. Recently the idea has been put forward that it is a variety of lichen planus. Dr. Dowling has described a case in which lichen planus was followed by typical lichen nitidus several months later, and Ellis and Hill (*Arch. Derm. Syph., Chicago*, 1938, 38, 569) at the Johns Hopkins Medical School published a paper in 1938 in which it was stated that 7% of their cases of lichen planus showed lichen nitidus-like lesions.

Cases of lichen nitidus recorded in *Proceedings of the Royal Society of Medicine*: Barber, H. W. (1924) 17, *Derm.* 39; (1925) 18, *Derm.* 45, 51, 68; (1926) 19, *Derm.* 35; (1927) 20, 1052; (1931) 24, 677; Dowling, G. B. (1926) 20, 91; Gordon, H. (1939) 32, 566; Klaber, R. (1937) 30, 1056; Sibley, K. (1931) 24, 395.

Major N. M. Wrong, R.C.A.M.C.: As you will remember the papule of lichen nitidus consists of a small granuloma lying immediately below the epidermis. The infiltrate consists of lymphocytes with epithelioid cells and giant cells and in many cases it is difficult to tell the difference between the histology of lichen planus and lichen nitidus. A biopsy was taken from the right cubital fossa and we tried to excise three typical papules. There is one point in the clinical appearance which I should like to mention and that is the lesions in the palms of the hands. Dr. Barber has drawn attention to these lesions in lichen nitidus. As far as I am concerned it was an entirely new concept.

Major Wrong then showed some slides.

The President: They are very typical sections, from what I remember of lichen nitidus.

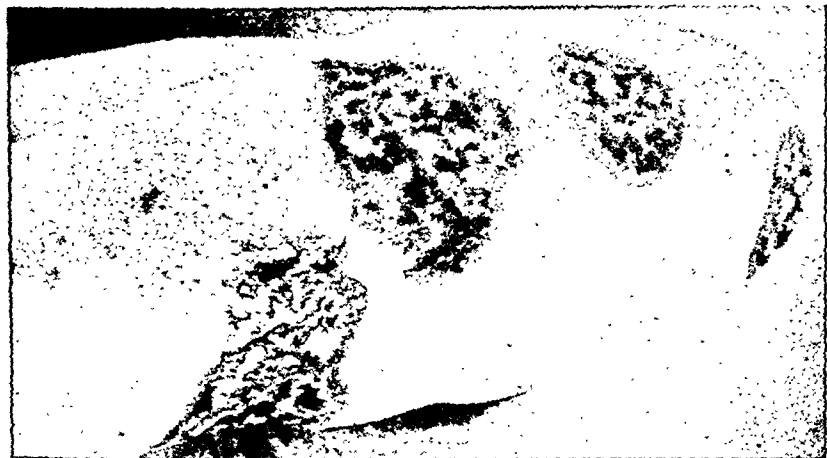
Dr. I Muende: I think that the histology differs from that described by Pinkus in that the lymphocytes are arranged diffusely within a fine network of fibrils, whereas typical sections of lichen nitidus show a relatively dense collection of cells, within one or two widened papillae, impinging on the basal layer.

Dr. Dowling: Barber showed at these meetings some years ago an exactly similar case, possibly more than one, and I published an account of one a little later. Those cases and the one shown to-day have remarkably constant clinical and histological characteristics, including their distribution. I think Barber was probably the first to point out the almost vesicular-looking spots in front of the wrists and encroaching on the palms; they are a very striking feature of Major Wrong's case.

Cutaneous Lipoidosis (? Xanthoma Eruptivum).—Major A. B. LOVEMAN, U.S.A.M.C. (introduced by Dr. W. FREUDENTHAL).

I. L., male, aged 37, was admitted to hospital on December 1, 1944, with a pruritic skin eruption of two months' duration. It began as small papules which gradually became yellowish and disappeared leaving a yellowish-tan discoloration. Believes he had a

There are ten active superficial granulomatous ulcers varying from $\frac{1}{2}$ in. up to 4 in. in diameter, situated mostly on the upper arms and chest. The edge is slightly undercut and bluish-red, and the base shows a tendency to scale and crust (see fig.). There is pus present



Ulcers on right upper arm, showing large size and somewhat irregular outline. [Photograph by Mr. Kenneth Titterton.]

in places. There are numerous oval or round, papery scars on the back $\frac{1}{2}$ in. to 1 in. in diameter, chiefly over the shoulders and presumably due to ulcers long since healed. He is well otherwise but has five very bad carious tooth stumps in the lower jaw.

There is no general enlargement of lymph glands or spleen, and the patient appears well in other respects.

Blood-count.—Red cells 4,400,000 per c.mm.: Hb. 90%; C.I. 1.02. Leucos. 11,000 (polys. 8,965, lymphos. 1,815, monos. 165, basos. 55).

Wassermann negative.

Biopsy: This showed granulation and scar tissue with some pus cells. Cocci were fairly abundant, but no tubercle bacilli were seen, and no reliable evidence of tubercle found.

X-ray of chest: Generalized emphysema.

Mantoux reaction: Human 1/1000 1 in. wheal, bovine 1/1000 1 in. wheal, i.e. positive.

Postscript (12.7.45).—Films and cultures have repeatedly yielded no fungus even with special culture media, but *Staph. aureus* has been grown on several occasions. Treatment, including sulphonamides locally and by mouth, has had little effect so far, and the lesions are still extending. Local penicillin gave only slight temporary improvement. —C. H. W.

The President: This case reminds me very much of a lesion on the hand of the horse slaughterer I recently treated. Eventually when we got the sepsis cleared up this turned out to be a classical lupus vulgaris.

Dr. Whittle: Would you get this large number of healed lesions on the back? That is one of the most difficult things to explain in this case—the large number of healed scars which presumably are the remains of similar ulcers.

The President: The fact that they have cleared up so completely is against lupus.

Dr. J. E. M. Wigley: I would like to suggest the possibility of the lesions being artefacts.

Dr. Whittle: It would be difficult to produce artefacts on both shoulder blades and down the back.

The President: People with artefacts usually wish to be treated, and he has not sought medical aid until now, after twenty-five years of illness.

Dr. G. B. Dowling: I am reminded of a condition described as pyodermitis chronica ulcerativa, a name which certainly fits this case, which was shown at the International Congress at Copenhagen 1930 (Proceedings, p. 1198). It has often struck me since that that condition might be related to acne conglobata, and that it might represent, as acne conglobata has been thought to do, a special type of reaction to *Staphylococcus pyogenes*.

A Member: Might I suggest blastomycosis, although the lesions are not as dry as usual? If this man were in California and had had his lesions for a less period of time we would think of coccidiomycosis, but we would not expect the man to have the lesions very long.

fat but absence of foam cells in the stained sections. There is, however, much against such a diagnosis. The cases previously described revealed definite liver damage and were jaundiced. Although our patient had a definite intolerance to fatty foods, he has never been icteric and all liver function tests were normal.

The help of the laboratory in cases of this kind is obvious. Both the blood chemistry findings and the demonstration of abnormal fat in the sections have clinched the diagnosis. We do not feel that the diagnosis of xanthoma eruptivum is entirely accurate or adequate in this case but for lack of a more suitable name it has been presented as such.

REFERENCE

THANNHAUSER, S. J., and MAGENDANTZ, HEINZ (1938) "The Different Clinical Groups of Xanthomatous Diseases: A Clinical Physiological Study of 22 Cases", *Ann. intern. Med.*, **11**, 1662.

Dr. W. Freudenthal: Major Loveman's careful investigations show that his case belongs to the group of cutaneous lipoidoses which in spite of many attempts still defy a satisfactory classification. An important point was the fading of the lesions when the cholesterol content went down and the reappearance when it went up. Histologically frozen sections stained for fat show the capillaries in the papillary body studded with very small fat droplets; there are no foam cells, a picture that one often meets in the "eruptive" forms of xanthoma. I don't mind admitting that seeing the case to-day, I probably would have missed the diagnosis, even if I had made a biopsy, because the paraffin sections do not suggest the presence of fat which the frozen sections reveal.

Colonel D. M. Pillsbury, U.S.A.M.C.: I had the opportunity of seeing this patient with Major Loveman about eight months ago. At that time the appearance of the lesions was rather different from that observed to-day. The yellow colour was more apparent, and many of the lesions had small crusts at their summits, whether as a result of scratching or an inherent inflammatory element in the process we could not determine. While the clinical picture in this patient is unusual, there seems no question that a diagnosis of lipoidosis is correct, and it is more nearly xanthoma eruptivum than anything else. I am rather relieved that Major Loveman and Dr. Freudenthal have not seen fit to attach a new name to this condition, because that has seemed the current fashion in connexion with lipid diseases during the past decade, and the classification has become extremely complex and confusing. I should like to ask if a fat-free diet has been tried in this patient.

Major Loveman: No.

Colonel Pillsbury: In view of the fact that there has been a tendency to waxing and waning of the lesions in this patient, it is possible that a relatively fat-poor diet might be of value though difficult to maintain under conditions of military service. Occasionally the results of such dietary management are quite striking. I recall particularly a patient of Urbach's who had been placed on an acidotic regimen for epilepsy, including a high fat diet. While on this diet he developed xanthoma, along with some relief from his fits. He was then put on a fat-free diet, with diminution of the xanthoma eruption and increase in frequency of seizures. The patient was in the dilemma of selecting either fits or xanthoma and, needless to say, he chose the latter.

Epithelioma Adenoides Cysticum.—C. H. WHITTLE, M.D.

W. N., aged 53. An agricultural labourer. History of tumours around the eyes and nose since the age of 16. There are a very large number of pearly tumours varying from pin-head size up to one tumour (now removed) $\frac{1}{2}$ in. diameter and approaching $\frac{1}{2}$ in. above the surface on the upper lip. The tumours are most numerous on the forehead and sides of the nose and in the central part of the face.

Family history.—His mother has a similar condition of the face, and one niece has the same trouble, apparently starting, in her case, at the age of 21.

Biopsy (sections shown): *From small lesion on forehead.*—A large cyst situated near the mouth of a sebaceous gland filled with keratinous material. The epidermis is stretched over this and the underlying sebaceous glands, and deep to these are spherical masses of basal-type cells arranged in palisade fashion in a rather hyaline stroma. There are other smaller cysts in the superficial part of the corium similar to the large cyst mentioned above.

Section of nodular tumour removed from left upper lip. The histology is similar to the section already described, there being grouped masses of basal-type cells with a considerable tendency to degeneration in the centre of the groups. The picture is of a more advanced condition of the same process seen in the section described above.

Multiple Chronic Ulcers of the Upper Arms and Trunk. (?) Cause.—C. H. WHITTLE, M.D.

D. H., aged 60. A ditcher. The history is of twenty-five years' ulceration on the forearms and upper trunk. The patient has never been abroad.

There are ten active superficial granulomatous ulcers varying from $\frac{1}{2}$ in. up to 4 in. in diameter, situated mostly on the upper arms and chest. The edge is slightly undercut and bluish-red, and the base shows a tendency to scale and crust (see fig.). There is pus present



Ulcers on right upper arm, showing large size and somewhat irregular outline. [Photograph by Mr. Kenneth Titterton.]

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A Member: Might I suggest blastomycosis, although the lesions are not as dry as usual? If this man were in California and had had his lesions for a less period of time we would think of coccidiomycosis, but we would not expect the man to have the lesions very long.

The President: Dr. Dowling, you showed a case of blastomycosis to the Section?

Dr. Dowling: That was a case of blastomycetic dermatitis of Gilchrist who eventually died of systemic blastomycosis. The primary cutaneous lesions were indolent-looking discoid granulomata, covered with little papillomatous excrescences from the interstices of which little beads of pus could be expressed.

The President: I remember one case which I diagnosed as blastomycosis about twenty years ago, which cleared up with treatment.

Dr. Whittle: Did these cases contract their condition in this country or elsewhere?

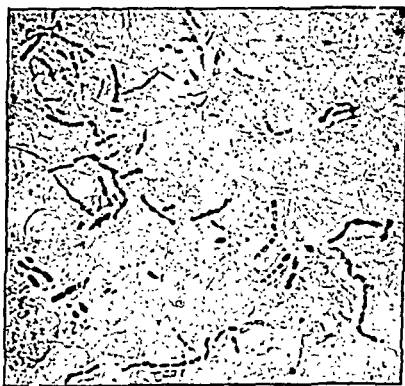
A Member: I have heard of a case recently diagnosed which looked like an animal ring-worm. It was a tumour with an inflammatory area over the back of one hand, covered with intradermal pustules. It was claimed that a culture had been grown.

Dr. Dowling: I have recently seen another case of blastomycosis from the Middle East. It was a flat granuloma with numerous small sinus-like openings from which pus could be expressed but without any warty excrescences. The diagnosis was made and confirmed in the laboratory by Air Commodore Morton. The patient was treated successfully by excision and skin graft.

The President: My case occurred about twenty years ago. I do not think he had ever been treated. It was soon after Dr. Dowling had shown his case. I inquired whether my patient had anything to do with opening packing cases from America, but he had not.

Erythema Annulare Centrifugum (Darier).—C. H. WHITTLE, M.D.

W. S., married woman, aged 36. A clerk. There is a two years' history of recurrent eruption on the thighs, consisting of large, bright red rings on the anterior aspect of the thighs with slight scaling; and a cluster of vesicles on the right sole. The skin trouble starts in February or March of each year and persists until the autumn. When first she was seen (6.9.44) the rings were 4 in. or more across. 6.9.44: Scales and scrapings taken from the rings showed no fungus after long search; also scales from early follicular lesions showed no fungus. However, the roofs of the vesicles on the foot showed abundant fungus with rather stout curly hyphae, breaking up into arthrospores and showing branching (*see fig.*). Cultures have remained sterile.



Scales from vesicle on foot showing abundant fungus elements. $\times 180$. [Photomicrograph by Mr. W. P. Hudson.]

The lesions reappeared in February 1945, and she now (5.3.45) shows a ring 1 in. diameter on the left thigh near the hip; another early, oedematous, lesion on the outside of the left thigh; a third small ring on the left shoulder; and a fourth ring starting on the right thigh. There are also a few healing vesicles on the outer side of the right sole.

She notices that her scalp has again become scurfy, and she states that it usually does so about the same time as the rings and vesicles appear. 12.3.45: Scales taken from the rings again show no fungus. The roofs of the vesicles on the right sole show abundant fungus as before.

The President: With regard to your case of erythema annulare centrifugum, will you please let us know what your researches produce? Perhaps you would treat the ringworm fungus and let us know what happens then?

POSTSCRIPT (14.4.45).—I now have cultures taken from vesicles on the feet which show *Trichophyton gypsum (asteroides)* in pure culture.—C. H. W.

Mycosis Fungoides.—H. CORSI, F.R.C.S.

E. S., male, aged 56, in good general health. Covering the trunk and limbs there is an eruption of striking geographical pattern. There are channels of normal-looking skin sharply demarcated from the abnormal, as one sees in psoriasis, though the general pattern is not that of psoriasis.

Examined more closely the rash is found to consist of erythema and infiltration, both a good deal more marked at the periphery of the affected areas, immediately before transition from the normal skin.

The patient states that new places become affected, and, conversely, affected areas return to normal.

There is a slight erythema of the face. On the scalp there is erythema without obvious infiltration, and there is no scaling. There is a very slight scaling elsewhere, such as one expects to see in most chronic inflammatory processes in the skin.

Hands, nails, and mucous membranes are normal.

The eruption has been present on the legs for thirty or more years and has tended to extend slowly upwards. In the last year the spread has been rapid, reaching the extensive distribution now seen.

Until a year ago there was no itching, but now the patient suffers sudden severe paroxysms of itching spreading all over the body several times a day.

The blood gives a normal red and white differential count and the Wassermann is negative. Microsection shows a pleomorphic infiltration with a preponderance of lymphocytes.

Dr. C. H. Whittle: I showed a case (*Proc. R. Soc. Med.*, 1940, 33, 580) with geographical lesions, as in Dr. Corsi's case, in a man about the same age and the Section made a tentative diagnosis on the biopsy and on the clinical picture of mycosis fungoides. The lesions completely disappeared. I have shown him since in a relapse (*ibid.*, 1943, 36, 612) and there is no doubt whatever that it is a case of mycosis fungoides. I saw him two days ago, he is still well and as his eruption commenced in 1939, there is a history of six years. On one occasion he was very ill indeed with generalized exfoliative dermatitis, and he has at times developed a few tumours which responded to X-rays. He nearly died of pneumonia in the exfoliative stage.

Another case, in a man aged 67, shown by me in 1933 (*Proc. R. Soc. Med.*, 1933, 26, 1558) gave a history commencing 1928, and is now alive and well seventeen years later. He also developed tumours which resolved with X-ray treatment.

These cases in their early stages are often difficult to diagnose; they may have severe and prolonged active phases with typical lesions, and some may apparently recover completely.

The President: The infiltrating cells were mostly lymphocytes and the pathologists would not admit that it was mycosis fungoides. There is no doubt that that condition can persist for many years. We have had cases at Bart's diagnosed elsewhere for many years as psoriasis which turned out eventually to be typical mycosis fungoides.

Plexiform Neuroma of Tongue.—J. E. M. WIGLEY, M.B., and I. MUENDE, M.R.C.P.

R. C., girl, aged 15. Lesions since the age of 2. She complains only of pain on biting her lip or her tongue. Probable onset of puberty (delayed). She is said to be of quite average intelligence. She is rather a sallow-looking girl with an underhung jaw and thick lips, giving a somewhat negroid appearance.

General medical investigation, including biochemistry, showed no abnormality.

W.R. negative.

About the inner surfaces of the lips and on the anterior third of the tongue are raised, glistening, yellowish nodules, varying in size up to that of a glass-headed pin. A similar small lesion was present on the lower edge of each upper eyelid and there was one lesion on the forehead. No areas of pigmentation, papules, or nodules (suggestive of von Recklinghausen's disease) were discovered on any other part of the body.

This case appears to be identical with the one described by Froboese. *Virchows Arch.*, 1922, 240, 316.

Dr. I. Muende: The skin shows large bundles of myelinated nerve fibres in the sub-epithelial tissue and among the adjacent muscle fibres. The perineurium is thickened but there is no appreciable change of the endoneurium. The tumour conforms with that of a plexiform neuroma.

I sent the section to Dr. Greenfield who reported: Sections of the neuroma of the tongue stained for myelin by modified Weigert-Pal method, and by the Gros-Bielschowsky technique, show numerous fairly large bundles of myelinated nerve fibres running in

the loose connective tissue of the subepithelial layer and among the more superficial muscle fibres.

The nerve bundles have a very thick perineurium, but no thickening or excess of endoneural tissue. There is no tendency in this area for the nerve bundles to break off into neuroma formation, although a few send small leashes of fibres towards the epidermis.

The tumour seems to fall into the group of plexiform neuromas, although these usually show more change in the endoneurium. The only endoneural abnormality in this case was the presence of some mucoid tissue within the perineurium, i.e. between it and the nerve fibres.

Dr. J. E. M. Wigley: There are no areas of pigmentation, nothing to suggest von Recklinghausen's disease.

Dr. F. Parkes Weber: The first description in England of plexiform neuroma of the tongue was that by Abbott and Shattock in a most elaborate paper which I well remember (*Trans. path. Soc. Lond.*, 1903, 54, 231). It was before the Pathological Society of London was merged into this Society and their case was a most remarkable one because the plexiform neuromatous disease was confined entirely to one-half of the tongue, so that it constituted a true "hemimacroglossia neurofibromatosa". Regarding the literature see F. P. Weber, *Quart. J. Med.*, 1930, 23, 162 (reference 11). In Dr. Wigley's present case the mamillated appearance of the distal portion of the dorsum of the tongue constitutes a striking feature.

The April and May meetings were held under the Chairmanship of Dr. Roxburgh.

The following cases were shown April 19, 1945:

- (1) Favus (With Culture).—Dr. J. E. M. WIGLEY.
- (2) Trichostasis Spinulosa; (3) Xanthoma in an Infant.—Dr. G. B. DOWLING.
- (4) Dermatitis from Cutting-oil resembling Riehl's Melanoderma.—Dr. HUGH GORDON.
- (5) Case for Diagnosis: ? Lymphocytic Reticulosis; (6) Bullous Eruption, Legs: ? Early Pemphigus; (7) Bullous Eruption: ? D. Herpetiformis.—Dr. G. DUCKWORTH.
- (8 to 10) Keratosis Follicularis; (11 to 12) Pityriasis Rubra Pilaris.—Dr. Z. A. LEITNER.

May 17, 1945:

- (1) Cutis Laxa; (2) Darier's Disease; (3) Acanthosis Nigricans Juvenilis.—Dr. SYDNEY THOMSON.
- (4) Boeck's Annular Sarcoid.—Dr. ALICE CARLETON.
- (5) Keratosis of Palms.—Dr. G. B. DOWLING.
- (6) Ichthyosis.—Dr. H. S. STANNUS (introduced by Dr. PROSSER THOMAS).
- (7) Morphaea of Glans Penis.—Dr. PROSSER THOMAS.
- (8) Epidermolysis Bullosa with Defective Development of Teeth.—Dr. H. J. WALLACE.
- (9) Dermatitis Atrophicans Diffusa.—Dr. THERESA KINDLER (for Dr. J. E. M. WIGLEY).
- (10) Carcinoma of the Breast; (11) Schamberg's Disease; (12) ? Lupus Erythematosus, ? Lichen Sclerosus et Atrophicus; (13) Pseudopelade of Brocq.—Dr. P. J. FEENEY.
- (14) Blue Pigmentation of the Face and Neck from Tattooing Owing to an Explosion.—Dr. H. C. SEMON.

Reports of some of these cases will appear in the *British Journal of Dermatology*.

Section of Surgery

President—SIR JAMES WALTON, K.C.V.O., M.S.

[April 4, 1945]

Treatment of the Retained Testis

By T. W. MIMPRISS, M.B., M.S., F.R.C.S.

THIS short paper is a "follow-up" of a group of patients with retention of the testicle who have been seen between the years 1938 and 1944 inclusive. Quite a large number on my records have not been adequately followed during this time and are therefore excluded.

When I started following this series in 1938 I believed, first, that spontaneous descent is a common occurrence especially round the age of puberty. Furthermore, that the type in which spontaneous descent is likely can usually be foretold on examination some time previously. Secondly, in the type of retained testis for which operation is necessary, that operation in most cases is best performed when the child is showing some signs of puberty development and the testis is a fair size and the cord a reasonable length.

In this series, therefore, I have tended to defer treatment until somewhere between the ages of 10 and 14. Examination at that age will usually demonstrate whether the testis can be pulled down in the direction of the scrotum, in which case spontaneous descent is likely; or whether the testis has come outside the external ring and is lying in the superficial inguinal position, in which case an operation is necessary. I have picked out the ones in whom I considered operation necessary, at about this age, when the development of the testis suggests that the operation will be easy.

On these lines the majority of patients sort themselves therefore into two main groups: (1) Those where spontaneous descent occurs. (2) Those in whom the operation of orchidopexy is not only necessary but easy.

There is left, however, a group in which the position is not quite clear owing to poor development of the genitalia or the inability to feel the testis. This group I have treated by hormone therapy followed if necessary by operation, and it is in this group that difficulties occur.

TABLE I.—SPONTANEOUS DESCENT

Case No.	Type	Age of descent	Remarks
1	Bilateral	13	Both down
2	Bilateral	12	Right down
3	Bilateral	14	Both down
4	Bilateral	14	Both down
5	Bilateral	13	Both down
6	Bilateral	12	Both down
7	Bilateral	10	Both down
8	Bilateral	9	Left down
9	Bilateral	12	Both down
10	Bilateral	14	Both down
11	Bilateral	14	Both down
12	Bilateral	14	Both down
13	Bilateral	13	Both down
14	Bilateral	14	Both down
15	Bilateral	13	Both down
16	Bilateral	9	Both down
17	Bilateral	11	Both down
18	Bilateral	12	Both down
19	Bilateral	14	Left down
20	Right	12	(operation right, aged 8)
21	Left	13	
22	Right	10	
23	Right	12	
24	Right	13	
25	Left	12	

Table I shows the number in whom spontaneous descent occurred in this series. It will be noticed that the age is usually in the neighbourhood of puberty and that a large number of these patients were referred with bilateral non-descent.

When first seen it was usual for them to have small testicles and a short cord, the testis slipping in and out of the external ring but showing no signs of turning outwards to a superficial inguinal position. As time went on development occurred and it was gradually possible to pull the testis down to the top of the scrotum, showing that there

was no organic reason why they should not go there. After that the stage of a migratory testis was entered, followed by the assumption of the permanent position of descent.

It should be emphasized here that no patient is included in this series in whom a migratory testis was found when first seen by me. I have had any number of these referred to me as cases of imperfect descent, but I do not put them on my records.

Table II shows the number of operations performed without previous employment of hormone therapy. Nearly all of these have been done at about the age of puberty, but in a few cases, owing to the presence of a troublesome hernia, operation has been put forward a year or two. Operation has been undertaken in these boys without previous hormone therapy because I have been satisfied that spontaneous descent will not occur

TABLE II.—ORCHIDOPEXY

Case No.	Type	Age of patient	Remarks
26	Left	14	
27	Bilateral	12-13	
28	Bilateral	12	
29	Right	8	Hernia
30	Bilateral	15	
31	Right	15	
32	Left	12	
33	Right	15	
34	Left	14	Two operations
35	Left	10	Hernia
36	Left	13	
37	Left	12	
38	Right	11	
39	Right	10	
40	Right	12	

and their development has been such as to make an operation satisfactory. In fact, nearly all of these were in the superficial inguinal position in which a good result should be obtained. All of these have given a good result in that a mobile testis of fair size is in the scrotum.

TABLE III.—HORMONE THERAPY

Case No.	Type	Age of hormone therapy	Result	Operation	Age	Result
41	Bilateral	15	Both down			
42	Bilateral	12	Both down			
43	Left	13		Orchidopexy	13	Satisfactory
44	Bilateral	13		Orchidopexy	14	Satisfactory
45	Right	13		Orchidopexy	13	Satisfactory
46	Bilateral	12		Orchidopexy	13-14	Satisfactory
47	Bilateral	14		Orchidopexy	14-15	Satisfactory
48	Bilateral	11		Orchidopexy	12-13	Poor. Two operations, both sides
49	Right	12		Orchidopexy	12	Poor. Testis at I.R.
50	Left	13		Orchidectomy	13	Testis atrophied

This group (Table III) contains 10 patients who, in my opinion, were neither obvious candidates for spontaneous descent nor for operation; the testis being very small and in some cases not palpable. These therefore received a course of hormone therapy. In 2 patients descent occurred following this and on the other 8 operation was performed, with a satisfactory result in 5.

In 2 of the unsatisfactory ones, the testis was never palpable and at operation it was found retained above the internal ring, and the cord was very short. As it was impossible to get the testis into the scrotum at the first operation, I tried leaving it at the external ring and operated again later in an attempt to get a good position. Case 48 has had two operations on both sides and the position of the testicles is still unsatisfactory. The same applies to Case 49, though it is possible that I shall be able to improve the position by a second operation. Both of these were mentally rather backward children and the retained testis was by no means the only abnormality which they possessed.

These two represent the difficult type which forms a small percentage of those seen. At present I think it is almost impossible to get a good result with a small testis and a short cord retained high up. Case 50 is, the only orchidectomy in this group. The testis which was lying at the internal ring was so atrophic that it was not worth preserving. It is possible that torsion had occurred at some time.

Spontaneous descent is a common occurrence, particularly around the age of puberty, and a good result can be obtained in suitable cases when orchidopexy is performed at about that age. There is no need to regard the imperfect descent of the testis as a condition for which treatment should be carried out as soon as possible. The type of treatment needed, if any, becomes steadily more obvious up to the age of puberty. At this age many will have solved their own problems; others will clearly need operation, and in a third group hormone therapy followed by operation is probably the best line.

The Value of Early Closure of Wounds

By D. F. FREEBODY, F.R.C.S.Ed.

EARLY closure of wounds is not a new treatment: it has been practised at various times during the last fifty years. Each time it has been discarded as a dangerous form of treatment. However, the great advantage of the treatment has been missed: if a wound can be closed successfully at an early date, return to function, and, in many cases, return to full function, will be assured in minimum time.

Burns and Young point out in their paper on the treatment of femur by closed methods (*Lancet*, 1945 (i), 236):

"In the 'Medical History of the War' Sir Anthony Bowlby quotes details of a series of 211 compound fractures of the femur treated by delayed primary suture, 161 being successful. He observes that the results were greatly improved in proportion as the practice of delayed primary suture increased. Closure diminishes the risk of all kinds of complications and gives rise to much more rapid union. In 1919 Pearson and Drummond were impressed with the importance of obtaining knee movements from the start."

These notes were written on experiences obtained during the last war, before the days of sulphanilamide and before Fleming had discovered the *penicillium notatum*. Such treatment could only be carried out under the most careful supervision because of the possibility of flaring-up of infection in soft tissue and joints.

In the period between the two wars, these valuable observations were forgotten, and no serious work was performed to ascertain the potentialities of this form of treatment in spite of the great advances made in chemotherapy. It was considered unsafe to suture a wound involving a compound fracture after six hours, even if careful excision and wound toilet were performed.

At the beginning of this war, British surgery was greatly influenced by the work of Trueta and his colleagues dealing with Spanish Civil War casualties. The treatment consisted of laying open the wound and surgical débridement, and enclosing the limb in plaster with the wounds left open: partial closure was practised in some cases. Infection was controlled by the administration of sulphonamides, &c. The oedema was reduced by the immobilization and even pressure exerted by the plaster, and subsided with healing of the wound, but this might be slow if at all extensive. This form of treatment undoubtedly saved innumerable limbs which would otherwise have had to be amputated. The great disadvantage was that slow healing of the wound gave rise to massive fibrous tissue formation, bone and tendons were exposed for long periods in the discharging wound with resultant sloughing and necrosis, and joints became stiff from immobilization and fibrosis.

Early closure of wounds is the natural evolution in wound surgery which keeps abreast of the discoveries and acquired knowledge of the properties of sulphanilamide and penicillin. The bacteriostatic properties of these drugs have gone a long way towards removing the danger of septicæmia and wound cellulitis. Infection due to staphylococcus, streptococcus and gas gangrene can be completely controlled in the vast majority of cases. These discoveries combined with new methods of resuscitation and blood transfusion render the patient a far more suitable subject on whom to try the lessons learned by earlier surgeons. This has been proved by Colonel Jeffries and his co-workers. Up to date these drugs have been used purely as defensive weapons against infection, and, as such, their value has not been exploited to the full.

The use of penicillin and early closure does not obviate full removal of all dead and infected tissue at the primary excision. Many of these wounds, if they reached the base hospital within a few hours of injury, can be primarily sutured under penicillin with absolute safety, but when they have been several days in transit without adequate observation and regular administration of penicillin, it is unwise to resort to primary suture. Delayed closure is carried out at the base hospital, ideally between the third and twelfth days. The administration of penicillin is started before the patient goes to the theatre and in cases of heavy infection, due to inadequate excision, a massive dose of penicillin or twenty-four hour course may be given first (depending on general condition). The wound is inspected, cleansed with saline or peroxide; any residual recesses examined for retained foreign bodies or completely loose bone, and a swab taken. The skin edges are freshened and freed; they are then sutured without tension. In wounds where the skin edges cannot be brought together without tension, and a large raw surface is left, closure is completed by the application of a Thiersch or split-skin graft, sutured to the periphery, and even pressure applied by flavine emulsion wool and a firm bandage.

By this combined method the complete closure of even the most extensive wound

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Section of Comparative Medicine

President—H. J. PARISH, M.D.

[April 18, 1945]

DISCUSSION ON THE CONTROL OF RICKETTSIAL INFECTIONS

Lieut.-Colonel C. H. Stuart-Harris: The rickettsial infections which are of concern in human medicine include a number of diseases affecting human beings in all climates and in most countries all over the globe. Biraud and Deutschman in 1936 listed 22 typhus and typhus-like fevers of rickettsial origin and more have since been added, but it seems probable that fuller knowledge of the rickettsias will enable ultimate simplification and re-grouping of this classification. The many common clinical characteristics of the typhus fevers and the common features of the rickettsias need emphasis as much as do the differences. Though transmission of infection is nearly always by insect or acarine vectors, the reservoirs of infection and type of vector differ in the various conditions. Control measures which are successful in some may not be applicable to other rickettsial infections, but it seems probable that the principles underlying these measures are common to all types. The practical application of these principles to epidemic typhus fever has recently achieved such spectacular results that it may be possible for considerable progress to be made in other rickettsial infections by similar measures appropriate to these conditions.

Principles of control of typhus fever.—The first principle of typhus fever control—attack on the vector by delousing of the infected population—is well known but introduction of potent chemical insecticides has now revolutionized field practice. So long as the destruction of lice involved the utilization of heat, it was impossible to deal quickly with very large numbers of people. Moreover, the undressing, disinfestation of clothes, and shaving of the hair were unpopular measures and added to the delay. The possibility of using an insecticide in a dusting powder was explored during the last war, but really efficient louse-killing agents are of comparatively recent date, and the newest types such as D.D.T. (Buxton, 1945) possess enormous advantages over earlier ones. The standard British Army delousing powder at the outbreak of war contained naphthalene, creosote and iodoform. Later derris root (rotenone) was used as the chief active constituent and the powder was known as A.L.63.

The efficiency of A.L.63 as an agent for killing lice quickly was undoubted as was that of the American Army's MYL powder which relied chiefly on pyrethrum for its activity (Davis and Wheeler, 1944). Then came the thiocyanates, including lauryl thiocyanate and Lethane Special 384. Lethane was used in the form of an impregnated belt to control body lice and an emulsion of thiocyanates was found to be extremely useful in the eradication of head lice (Busvine and Buxton, 1942). Thus far, however, none of the new insecticides had the power of local persistence so that treatment or impregnation needed to be repeated every few days or else reinfestation would develop. D.D.T. possesses this power of persistence of action to an outstanding degree and thus bids fair to take pride of place among insecticides. Though it has a relatively slow lethal effect on lice and does not kill nits, its persistence on skin or clothes is sufficient to guarantee freedom of the individual from reinfestation by larval lice hatching out from nits (Annand *et al.*, 1944; Scobbie, 1945) or from other individuals. It is not absorbed from the skin when applied in powdered form dispersed in inert powder (talc) and when used as a dry powder it is entirely harmless to man. The powder is applied to fully clothed individuals by using a dusting-gun of the type used in agriculture, forcing a cloud of dust up the arms and legs, down the neck and over the chest, axillæ and groins. A partial distribution of powder is adequate for delousing because of the migratory habits and selective location of the body-louse.

The second principle of control in typhus fever, based on the infectivity of the human cases and the fact that man constitutes the reservoir of infection, consists in early diagnosis and isolation in hospital. The newer methods of cultivation of rickettsias have produced relatively abundant quantities of rickettsial antigens for serological tests. Hope that these antigens would aid diagnosis at an earlier stage of the disease than that afforded by the Weil-Felix reaction has not, however, been fulfilled. Rickettsial agglutination and complement-fixation tests are now of established value in tracing the epidemics.

can be obtained. Penicillin is given systemically for five days. Local application of penicillin by means of tubes has been disappointing, the wound frequently breaking down and forming sinuses.

Advantages of early closure.—It is well known how indurated and scarred a limb may become around a chronic varicose ulcer or an extensive burn. The fibrous tissue forming under the granulating surface penetrates deep into the underlying structures. The pain from a raw surface prevents the patient from moving the limb, while contractions further limit joint movement. So also in the extensive soft tissue wound, as healing occurs a large scar will develop adherent to the underlying muscle.

It is practically impossible to keep a large granulating surface free from pathogenic organisms for any length of time. Any secondary infection developing is followed by fresh fibrous tissue formation. The depth to which this fibrous tissue may extend is seen at any operation on a raid casualty treated by the old methods. It may reach to underlying bone, binding skin, deep fascia and tendons down to bone, and make movement impossible.

Complete closure of a soft tissue wound will not only prevent reinfection of the wound but will also reduce the amount of scarred tissue formation to a minimum. Œdema of the tissue will be absorbed rapidly as soon as the source of irritation is removed. The patient's pain will be relieved and of his own volition he will start using his limb, and an earlier return to function is assured.

If the tissue can be drawn together by closure, the recesses in the wound will be shut down, thereby preventing the pooling of serum, blood or pus. The early movement of the muscles of the limb will help to express any such collection.

The protection of tendons can be assured by closure of the wound by complete suture. Where it is necessary to complete the closure by skin graft, an adherent scar may result, but this can be excised later and a full-thickness graft applied when the tendon has been saved from initial destruction. In the case of compound fractures early closure of the wound is absolutely essential to prevent secondary infection reaching the bone. If it should be necessary to swing skin flaps or make parallel skin incisions to retain tension on the main incision, these secondary incisions can be Thiersch-grafted.

Burns and Young have shown in cases of fractured femurs treated by control of infection and early closure of wounds that movements can be started immediately, alignment being controlled by weight traction (*Tr. of Fractured Femurs, Lancet, 1945 (i), 236*).

Wounds of the knee-joint demonstrate very clearly the value of early closure. It has been long known that the synovial membrane can look after itself as long as it is not being bombarded by infection from a source within or outside the joint. It is the damage to the soft tissues and bone that determines the ultimate functional result of a knee-joint injury. After surgical toilet of the wound and removal of the foreign body the synovial membrane is closed. The soft tissues must then be drawn together and the wound completely sutured or grafted.

Early closure by suture and skin graft will ensure minimal extra-articular scarring and rapid absorption of œdema and swelling. Throughout, the infection must be controlled by the administration of penicillin and sulphanilamide systemically. Fluid collecting in the joints is aspirated and penicillin is instilled into the joint to keep up the concentration of penicillin in the synovial fluid.

Failure to obtain a good result in cases of penetrating wounds of skin-joints is usually where there has been excessive bone damage (articular) and where, owing to soft tissue loss, the wound has not been closed.

Slides were shown illustrating the above principles and these were kindly lent by members of the Orthopaedic Unit at Botley's Park.

MEETING HELD AT THE LONDON HOSPITAL ON MAY 9, 1945.

The following cases were shown:

- (1) Multiple Calcified Hydatid Cysts of the Liver.—Mr. M. H. D. COOPER (for Sir JAMES WALTON).
- (2) Congenital Cystic Disease of the Liver and Kidneys.—Mr. MORGAN and Mr. A. WATERSON (for Sir JAMES WALTON).
- (3) Congenital Cyst of Common Bile Duct.—Mr. WILKINSON (for Sir JAMES WALTON).
- (4) Carcinoma of the Kidney Associated With Double Pelvis and Ureter.—Mr. COOPER (for Mr. NELIGAN).
- (5) Intestinal Fistula in an Obstructed Incisional Hernia with Sloughing of the Sac.—Mr. A. TURNBULL (for Mr. ALAN PERRY).
- (6) Femoral Embolectomy.—Mr. C. H. DE BOER (for Mr. FATHI).
- (7) Paget's Disease of Bone.—Mr. C. H. DE BOER (for Mr. NELIGAN).
- (8) Case of Peyronie's Disease.—Mr. J. FATHI.

summer. During 1943, widespread prevalence of typhus fever in the Egyptians and in the Arabs of North Africa exposed our armies to considerable risk of infection. Yet no general or localized epidemic occurred, even though some of the bitter fighting during the winter ranged around the typhus-stricken villages in the area round Constantine in Algeria. The reason for this low prevalence of typhus was obvious. The British Army achieved an astonishingly high standard of cleanliness from lice. This was effected by the ordinary measures of cleanliness and by using delousing measures including A.L.63 powder. Even when typhus did occur, lice were rarely discovered on the bodies of the patients and therefore no risk of spread within the units existed. The source of infection of these sporadic cases was obviously the civilian population because of the frequency with which cases came from base depots or dock companies employing large numbers of civilians. The disease itself in our troops was severe and carried a mortality rate of 30%. Comparison of our experience with that of the American Army in North Africa was most instructive. The American Army fighting alongside our own, with substantially similar hygiene precautions and similar risk of infection from civilians, experienced about a score of cases of typhus with no deaths at all during the period when our First Army had 41 cases with 13 deaths. The only discoverable difference between the two armies was that the American Army was wholly immunized with Cox vaccine. The difference in incidence of typhus in the two armies and particularly the absence of deaths from typhus in the American Army could only have been due to the immunization of the American soldiers with rickettsial vaccine.

General immunization with typhus vaccine began in the British Army in the late spring of 1943 and was extended to the Middle East Army at the close of the year. The civilian epidemic in the winter of 1943 to 1944 was much smaller than that in the previous winter but, when allowance is made for this, the Middle East Armies experienced a very much lower incidence of typhus with a much lower death-rate in 1944 than in 1943. The British First and Eighth Armies and the American Army passed over to Italy in the autumn of 1943 and were again exposed to infection from civilians during the Naples epidemic. The fact that only two British and two Americans contracted typhus during this outbreak confirmed the previous experience that combined louse-control and immunization was highly effective in preventing even sporadic cases of typhus. It is also significant that the anti-lice powder used by the British Army and by some thousands of civilians employed by the Army was the standard A.L.63 which was applied and reapplied to the clothes and bedding of the troops. The evidence in favour of the success of these Army control measures seems overwhelming but prophylaxis in the Army is a different proposition from controlling an outbreak in civilians once this has developed. The experience in Naples indicates that we can control typhus even in the face of an epidemic.

The Naples outbreak probably had its roots in the occurrence of sporadic cases in March 1943, but epidemic prevalence was not experienced until December. Lack of washing facilities, malnutrition, overcrowding and the use of air-raid shelters as actual living quarters were probably responsible for the epidemic, which began in the poorer sections of the town and particularly in the area in which large cavern-like air-raid shelters were located. Three hundred cases occurred in December and in this month the efforts of the Allied medical officers, Red Cross and civilian workers were aided by the arrival of workers of the International Health Division of the Rockefeller Foundation under the direction of Dr. F. Soper, and of the American Typhus Commission under the direction of Brigadier-General Leon A. Fox. A scheme for inspection of the contacts of notified cases and for case-finding by medical inspection of the crowded air-raid shelters, where 10,000 people were permanently housed, was put into operation. Many cases of typhus were found in these shelters, which were overcrowded, foul, and infested by lice, fleas and bedbugs. Delousing by powder-spray was the only measure of control applied to these people but cases of actual typhus were transferred to hospital after preliminary dusting. Pyrethrum powder was used at first but, as supplies became available, 10% D.D.T. powder was used.

The chart (fig. 1) shows that about January 10, 1944, a sharp fall in the incidence of typhus set in, and that from then onwards the epidemic slowly petered out. Allowing twelve days for the incubation period of typhus, the events occurring prior to December 29, 1943, were clearly crucial. The chief control measures applied during these closing weeks of December were case-finding and delousing of both immediate and remote case contacts. The principles of diagnosis and isolation of cases, and of throwing a cordon around each infected case by delousing both case and contacts with a persistent insecticide are thus the key measures to be taken during an actual epidemic. It is significant that though cases of typhus occurred in many villages outside Naples City, the application of these measures of diagnosis and of contact delousing were effective in preventing any subsequent epidemic in these areas. In Naples itself, the extended programme of the Typhus Commission

logy of the disease and in distinguishing epidemic from murine infection (van Rooyen and Bearcroft, 1943; Stuart-Harris, Rettie and Oliver, 1943; Plotz, 1943) but do not usually assist greatly in diagnosis. Early diagnosis and hospitalization have, however, been helped by bedside performance of the Weil-Felix test using the Castaneda slide agglutination test with a concentrated *Proteus* OX 19 suspension (Castaneda *et al.*, 1940). Colouring of the latter with methylene-blue enables a direct test of a drop of blood to be made and, in this way, confirmation of clinical diagnosis can be obtained in the patient's own home. Contacts and doubtful cases can be similarly examined and cases which would otherwise be missed may thus be detected and prevented from becoming a source of danger to others.

The third principle of typhus control, immunization by rickettsial vaccines, was discussed at a meeting of the Royal Society of Tropical Medicine and Hygiene in 1940 (Murgatroyd, 1940) and by this Society in 1941 (Findlay, 1941). So long as the methods of vaccine production were tedious, as in the case of Weigl's louse-gut vaccine, or the vaccines were possibly dangerous, as in the case of the living murine vaccines (Blanc and Baltazard, 1938; or Laigret and Durand, 1939), progress was slow. The Cox method of cultivation of epidemic rickettsias in the yolk-sac of developing chick embryos (Cox, 1938) enabled large quantities of a killed (formolized) vaccine free from unpleasant clinical reaction to be produced quickly. Almost at the same time, the French workers in North Africa, Durand and Giroud (1940), introduced a mouse-lung vaccine of killed formolized epidemic rickettsias and by using rabbits (Durand and Giroud, 1941) and sheep (Horrenberger and Renoux, 1943) were able to produce quantities sufficient for mass use. When typhus research was first begun in 1941 by workers at the laboratories of the Medical Research Council and in the Army, it was felt desirable to investigate the relative efficiency of these yolk-sac and mouse-lung vaccines. The antigenic structure of the rickettsias was also studied in an effort to determine whether any diversity of antigens existed other than the known differences between epidemic and murine strains (Zinsser and Castaneda, 1932). Soon after these studies began, Craigie (1942) developed a method of purification of the yolk-sac culture of rickettsias by ether-treatment which resulted in a considerable concentration and separation of the rickettsias from unwanted egg-yolk. Craigie's vaccine also differed from commercial vaccine in that it was composed of pooled cultures of three rickettsial strains—a murine, a recently recovered strain from the Madrid epidemic, and the old classical Breinl strain first recovered in Poland in the 1919 to 1921 outbreaks. Immunization has now been in use in the British Army on a considerable scale since 1943, and in the American Army for an even longer period. Much of the vaccine used by the British Army has come from Craigie's laboratory but some has been supplied by commercial firms in the United States. The necessities of war have denied us the chance of obtaining reliable statistical data on the effect of immunization on the incidence of typhus. However, laboratory experience (Topping, 1944; Wöhlrab and Patzen, 1944) and some field experience (Ding, 1943; Schulten, 1944) have indicated that immunization effects a real lessening of the severity of disease and reduction of mortality from typhus. The field experience which I shall now detail confirms this and also suggests, though it does not prove, that reduction in incidence is effected by immunization.

Recent field experience of typhus in relation to methods of control.—The experience of the Allied Armies since 1942 enables us to say emphatically that the bogey of louse-borne typhus no longer threatens a disciplined community such as an army. This is a tremendous achievement, for typhus has always been a disease which flourished in armies and under wartime conditions. Table I shows the experience in the British Army as regards

TABLE I.—TYPHUS FEVER IN THE BRITISH ARMY

Area	Period	Number of cases	Deaths
(a) <i>Prior to immunization with typhus vaccine</i>			
Middle East	January to June, 1943	134	44 (33%)
	July to September, 1943	57	1 (2%)
		(High proportion of murine cases)	
North Africa	January to April, 1943	41	13 (32%)
(b) <i>After immunization with typhus vaccine</i>			
Naples	January to March, 1944	2	1
Middle East	January to June, 1944	10*	2 (10.5%)

* The civilian epidemic in the Middle East in 1944 was on a considerably reduced scale compared with that in 1943—typhus before and after the introduction of general immunization with the Cox type of typhus vaccine. The studies of van Rooyen in the Middle East (van Rooyen and Bearcroft, 1943) indicated that typhus there was predominantly of epidemic type during the winter seasons but that murine typhus with characteristically low mortality predominated in the

summer. During 1943, widespread prevalence of typhus fever in the Egyptians and in the Arabs of North Africa exposed our armies to considerable risk of infection. Yet no general or localized epidemic occurred, even though some of the bitter fighting during the winter ranged around the typhus-stricken villages in the area round Constantine in Algeria. The reason for this low prevalence of typhus was obvious. The British Army achieved an astonishingly high standard of cleanliness from lice. This was effected by the ordinary measures of cleanliness and by using delousing measures including A.L.63 powder. Even when typhus did occur, lice were rarely discovered on the bodies of the patients and therefore no risk of spread within the units existed. The source of infection of these sporadic cases was obviously the civilian population because of the frequency with which cases came from base depots or dock companies employing large numbers of civilians. The disease itself in our troops was severe and carried a mortality rate of 30%. Comparison of our experience with that of the American Army in North Africa was most instructive. The American Army fighting alongside our own, with substantially similar hygiene precautions and similar risk of infection from civilians, experienced about a score of cases of typhus with no deaths at all during the period when our First Army had 41 cases with 13 deaths. The only discoverable difference between the two armies was that the American Army was wholly immunized with Cox vaccine. The difference in incidence of typhus in the two armies and particularly the absence of deaths from typhus in the American Army could only have been due to the immunization of the American soldiers with rickettsial vaccine.

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including case-finding, contact delousing, mass delousing, immunization of key personnel and of contacts effectively continued and completed the control. However, though enormous numbers of people were deloused, including 60,000 persons a day at the peak

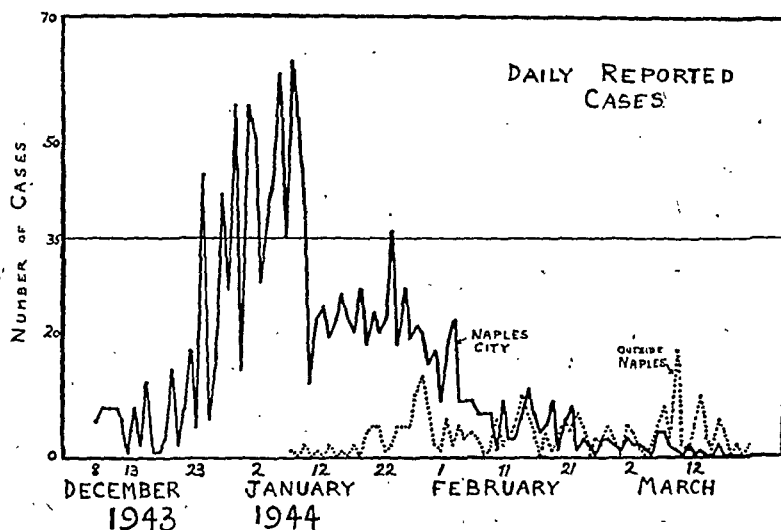


FIG. 1.—Typhus epidemic, Naples (1943-44)

of the campaign, lousiness continued to be present as was shown by a house-to-house study carried out in March. By then, however, the typhus had been controlled because the rickettsia-infected lice had been largely eliminated. The role of immunization in the civilian population was clearly unimportant. Some few cases occurred in medical or nursing personnel who had been immunized but all recovered satisfactorily. In spite of bad conditions for reception of patients and delousing in the civil hospitals, few infections were contracted by the staff and the factor of infection by inhalation appeared to be unimportant.

In conclusion, the wartime experience of at least one rickettsial disease has afforded solid grounds for belief that logical principles of control of rickettsial infections are well founded. Louse-borne typhus has been, to all intents, abolished from the Army. Its control in the civilian population is possible if adequate resources are made available. A nation-wide epidemic would clearly be a more formidable problem than the relatively circumscribed Naples epidemic. If there are enough trained people to hunt out the foci of infection, however, and if D.D.T. is forthcoming in sufficient amount, the result of a nation-wide campaign should be as successful as was that carried out in Naples last year.

I am indebted to the Director of Hygiene, Major-General D. T. Richardson, C.B., M.C., K.H.S., and to the Consulting Physician to the Army, Major-General A. G. Biggam, C.B., O.B.E., K.H.P., for help in the preparation of this paper.

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Dr. J. Carmichael opened the discussion from the veterinary angle, dealing first with heartwater in cattle, goats and sheep, a rickettsial infection of importance in parts of tropical and South Africa, and transmitted by ticks. The disease is characterized by accumulation of fluid in the pericardial sac and the causal organism, *Rickettsia ruminantium*, is found in the cytoplasm of endothelial cells of the capillaries of the renal glomeruli and parts of the brain. Vaccines, serum and chemotherapy have not proved successful and control measures are directed against the tick, the animals being treated by repeated dipping in arsenicals at suitable intervals.

So-called "tick typhus" in dogs might be important in view of its possible transmission to man by the dog tick. The pariah dog is largely responsible for maintaining a reservoir of infected ticks. Ticks on domestic dogs are readily destroyed by the use of derris, pyrethrum or arsenical washes.

Dr. R. Lewthwaite: *Control of scrub-typhus*.—This disease is an acute infectious fever, of some fifteen days' duration caused by *Rickettsia tsutsugamushi*, which is inoculated into the victim by the bite of larval mites, *Trombicula akamushi* in Japan and Formosa, *Trombicula deliensis* in Malaya, and morphologically similar mites in the South-West Pacific zone. The virus is transmitted through the egg in all of them. The larval mites feed predominantly on wild rodents, field voles or rats, and in so doing may either derive their infection from them or, if already infected, inoculate the infection into them. The nymphal and adult forms are, as far as we know, entirely vegetarian. On several occasions wild rats have yielded laboratory strains. Larvae of *Tr. deliensis* have also been taken from certain migratory birds, such as *Acrocephalus orientalis*, which migrates southward from Japan in the winter, and may therefore carry the virus to distant countries. The all-important maintenance of the disease in nature is a rickettsia-mite-rodent cycle. Scrub-typhus is none other than tsutsugamushi, long known to have its classical home in Japan and Formosa. Research during the past two decades has established this identity beyond dispute. The term "scrub-typhus" is thus invalid but it has come to stay for wartime usage. As a descriptive term "scrub-typhus" has some merit. Concerning "scrub", the disease has occurred chiefly in areas of secondary jungle, areas once cleared from forest and cultivated with millet or other grains, and later become overgrown with secondary shrub-growth. Infested areas are usually overrun with rats, and it is likely that these have been attracted by the ready food supply afforded by grain cultivation and have thereby seeded out the virus.

Areas once infected frequently continue to harbour the virus, at least for as many years as our records exist. They are often very circumscribed in extent. The recently-coined term "scrub-typhus island" is therefore a most useful expression of these features. It will readily be realized that in one sense the disease is a "place disease" and that in another sense it is an "occupational disease", in so much as those who enter infected areas for recreation or to work are at risk, and they comprise the vast majority of victims. It follows also that scrub-typhus, unlike its Western louse-borne counterpart, is mainly a disease of the countryside, not of the town.

Concerning "typhus", the disease in its clinical syndrome, its causal organism, its human pathology and its serology is akin to the other three groups of the typhus-like fevers, viz. louse-, flea-, and tick-borne. Thus clinically the syndrome is much the same; save that, in some 50% of European cases and a smaller percentage of the cases in the darker-skinned Asiatics, a small necrotic ulcer develops at the site of the bite. Its causal organism is a rickettsia. Only the most expert pathologist could distinguish between the morbid anatomy and morbid histology of louse-borne and mite-borne typhus, as examination of human tissues of the former brought from Naples by Dr. van den Ende and from Egypt by Dr. Russell Amies has indicated. Convalescent serum agglutinates one of the strains of Proteus X bacilli, although it is the XK strain, not the X 19 strain. But in its epidemiology and its experimental pathology it differs widely from the other three groups of the typhus-like fevers, so that counter-measures now so happily advanced in refinement and effectiveness against louse-borne typhus fail against mite-typhus.

Past history.—A Chinese writer of the sixteenth century described a disease that corresponds closely with the scrub-typhus, and attributed it to the bite of a sand-mite, which mite Japanese workers later identified with the *Tr. akamushi*. In pre-war years it was known in all territories that are included in an arc drawn on the map from Assam and Burma southward, eastward and then northward to Japan, i.e. including Ceylon, Malaya, the Netherlands-Indies, Queensland, the Philippines and Formosa; it will thus be encountered all the way to Tokyo. On the whole it was then more interesting than devastating and not to be compared with malaria, tuberculosis, lobar pneumonia, and dysentery as a scourge of populations. It did, however, cause occasional concern to planters and

others whose vocation took them into scrub-land. The mortality varied—in Japan, in some districts, it was as high as 60%, in others 30%, in Malaya and Formosa 15%.

Present.—Since the outbreak of the Japanese war scrub-typhus, both by its higher incidence and its psychological effect on troops, has compelled the institution of energetic investigation and counter-measures in all zones of that theatre of war. The reason for this derives from its "occupational" character. Where one man previously was exposed, a thousand are now exposed. Man's irruption into the haunts of this rickettsial disease of mites and small rodents has of necessity, and to his cost, caused him to supplant the rodent to some extent as a host of the mite, and thereby to become the indicator of hitherto "silent" scrub-typhus islands.

Concerning incidence and mortality and counter-measures, I am unable for reasons of security to give details; suffice it to say that one or more men of the Allied Armies die every day from the disease; and that one-third of those who recover do not return to the front line.

Future.—This, of course, rests with the success of counter-measures, which may conveniently be grouped under the headings anti-rat, anti-mite and anti-rickettsial.

Anti-rat: In Malaya, Kingsbury and Paranjothy investigated the possibility of reducing the rat population on plantations by the use of "rat viruses" of various types; but met with little success. Certain of these viruses proved innocuous to the local rats. In "herd" experiments, certain others were at first effective, but later became progressively ineffective. Organized rat-hunts on estates effected a temporary reduction in the rat population, but any cessation of effort resulted in its speedy restoration to its former level.

Rats trapped or killed in the vicinity of camps should be burned, to ensure destruction of their mite parasites, for the mites will rapidly leave the dead rat and we do not yet know whether a partially engorged larval mite will complete its feed on another host (which might well be man under these circumstances) before moulting.

Anti-mite: Many such counter-measures, some of proved worth, others awaiting evaluation, may be grouped under the heading of Mite-avoidance. Such are: the use of immune labour in the clearing of scrub, and the "civilizing" of an area, such as a camp-site, by the cutting of paths, the liberal use of sand, and so forth. The use of bulldozers and flame-throwers in clearing camp-sites suspected to be infested will probably achieve the same end, viz. avoidance of close contact with the scrub by susceptible subjects.

Intensive investigation of mite-repellants or mite-poisons has been made, especially by a team of Australian entomologists led by McCulloch. They have been successful in discovering and evaluating certain mite-poisons that are now in extensive use in the field, and form our most proved weapon against scrub-typhus.

Anti-rickettsial: Chemotherapy and serum therapy have not as yet met with any success; the former has had recent extensive trial, the latter less so. Inability to apply these measures before the fourth or fifth day after onset of the clinical symptoms probably accounts for their failure to modify the course of the disease.

Of vaccine prophylaxis suffice it to say that the welcome advent of new minds and new methods in many laboratories in this aspect of scrub-typhus control has greatly speeded progress.

Lastly, the results of "forward nursing" must be stressed. In the appalling monsoon country in which much of the jungle-fighting has hitherto occurred, evacuation of the sick from the most forward areas by road would involve such journeys as four days in a jeep at four miles an hour. And since this infection throws a great strain on the heart, the disadvantages of such a mode of evacuation will readily be realized. Rapid air-evacuation, where air-strips are plentiful and the weather favourable, provides one alternative, but in monsoon weather such conditions may not obtain. The institution of "forward nursing", i.e. the sending of trained nursing sisters much further forward than is usual, so that the patients can be nursed expertly in situ, has proved very successful. The nursing sisters welcome the opportunity and many men undoubtedly owe their lives to them.

The President inquired whether (a) convalescent serum or (b) any other antiserum had been useful in treatment.

Dr. Forrest Fulton described the work carried out at the National Institute for Medical Research on the testing of murine rickettsial vaccines and described the studies of the antigenic relationships of epidemic and murine rickettsiae. An effort was made to standardize rickettsial vaccines by a counting technique, and, when this was done, vaccines made from yolk-sacs or from lungs of rodents gave similar degrees of protection.

Of the various methods used to evaluate the vaccines, the most satisfactory had been that based on a test devised by Dr. Craigie, in which mice were actively immunized against rickettsial toxin administered intravenously. Dr. Fulton discussed possible explanations of the observed antigenic differences between murine and epidemic rickettsiae, and suggested that the relationship with *Proteus* OX 19 was a heterologous one. He showed some lantern-slides demonstrating these points and also the appearance of purified rickettsial suspensions by visual light and under the electron microscope.

Dr. A. Felix said that a number of notable advances in the control of rickettsial infections had been made during the present war. The outstanding achievement in the prevention of louse-borne typhus was due to the entomologist and the chemist, and not to the bacteriologist. Undoubtedly D.D.T. was going to revolutionize the methods of typhus control. Another advance of great importance was the development of the various types of typhus vaccine.

Very little progress had been made with specific treatment with drugs or serum. Anti-rickettsia sera from the horse or the rabbit were very difficult to manufacture and in addition were very poor in OX 19 antibody. For this reason Dr. Felix suggested combined treatment with anti-rickettsia and anti-*Proteus* OX 19 serum. The latter is much easier to produce on a large scale. There is ample evidence to show that the heat-stable rickettsial antigens which correspond to the *Proteus* OX antigens are major antigenic components of the rickettsiae and cannot be disregarded in immunity to typhus. There is a striking analogy between the heat-labile and the heat-stable antigens of rickettsiae and the Vi and O antigens of *Bact. typhosum* and it is worth remembering that the efficacy of a therapeutic anti-typhoid serum also depends on the presence in it of the two corresponding antibodies.

Brigadier-General Leon A. Fox (U.S.A. Typhus Commission) said that during the epidemic in Naples D.D.T. was of great value. Its value lay in the fact that it not only killed lice; but that in addition it rendered an individual non-infectable for a period of three to four weeks. No other delousing agent accomplished this.

Vaccine, too, had proved of great value. He knew of no documented case where an individual who had been immunized with Cox-Craigie vaccine subsequently died of typhus fever. Vaccine was particularly important in long-range typhus control. When large numbers of a population were vaccinated, epidemics could not get started. All doctors, nurses and sanitary personnel should be vaccinated, for vaccine would save the lives of these highly exposed groups.

In the control of typhus fever two things were important—D.D.T. and immunization; and in the early stages of an epidemic a case-finding programme so that focal delousing might be instituted.

Mr. E. O. Longley described a fatal disease of unknown aetiology, known as "Nigerian dog disease", which fails to respond to treatment and to which country-born dogs are said to be resistant. He had examined a case which was said to be typical and the symptoms were: Persistent epistaxis, rhinitis, pyrexia, tachycardia, splenomegaly, anaemia and asthenia. At autopsy the viscera showed petechial haemorrhages and the spleen and lymph nodes were enlarged. No bacteria or protozoa were found. The picture suggested rickettsiosis.

The speaker also recounted his own experience of an attack of typhus following a tick-bite, the syndrome being typical, with petechial rash, and the Weil-Felix reaction was negative. Infection was thought to have originated from a country-born house dog. Previous human cases in West Africa have, probably on insufficient evidence, been ascribed to a murine source. It was advisable to consider the possibility of a canine reservoir as a source of human infection and also to search for rickettsial infection in cases of obscure febrile disease in dogs in the tropics.

Read by Dr. R. Lovell for Mr. Norman Hole: *Infectious kerato-conjunctivitis of cattle*.—This is a disease of the eyes occurring in cattle in this country which may be caused by a rickettsia; excessive lacrimation is followed by conjunctivitis, photophobia, and opacity of the cornea. Ulceration of the cornea may develop, and sometimes results in permanent injury or even complete blindness.

What was probably the same condition was described in this country as contagious ophthalmia, by Penberthy (1897) and Esmond Brown (1934), and as contagious keratitis by Craig and Ratter (1940). In South Africa Coles (1931) reported a similar condition caused by a rickettsia, and in Germany Wagener and Mitscherlich (1942) described European kerato-conjunctivitis or rickettsial disease of cattle. The evidence at present does not seem to justify the use of the word contagious.

In smears made from scrapings of infected conjunctivæ we have found inclusions in epithelial cells which closely resemble those described as rickettsiæ by Coles and by Wagener and Mitscherlich, but we are not so sure of their rickettsial nature. We have not been able to transmit the symptomatic disease to healthy adult cattle, but we have transmitted the inclusions. We have not, up to the present, tried calves, which have been successfully used by the German workers.

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The numbers involved are small admittedly and the project was an economic one, to help the Manager of the estate, and not specifically designed to demonstrate residual immunity, doubts as to which had not at that time been seriously raised. Yet the results do seem clearly to indicate that a residual immunity is the rule.

Dr. Lewthwaite added that he personally had never seen a case of a second attack in the same individual; nor had Dr. Fletcher in his series of cases. Yet second attacks are reliably reported by Dutch and Japanese workers, but almost invariably with the qualifying clause that such second attacks are usually much milder than the initial attacks.

Concerning the use of convalescent serum, raised by the President, Dr. Lewthwaite stated that his colleague, Dr. S. R. Savor, had hyperimmunized a horse over a period of two years, using eventually enormous doses of live virus by the intravenous route. Concentrated serum from this horse had been tried in laboratory animals, and had given a slight indication of efficacy but when later tried in human cases it had failed to modify the course of the disease, probably because one rarely had an opportunity to treat cases before the fourth or fifth day of the fever. But it may well have been, as Dr. Felix had suggested, that this type of serum was deficient in "O" antibody content.

The President said that considerable progress had been made in the control of rickettsial conditions, but much remained to be done. Full advantage should be taken of the exceptional opportunities now existing for the study of typhus and allied infections. Rickettsia were apparently responsible for a variety of diseases of veterinary as well as medical importance.

Section of Radiology

President—J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

[January 19, 1945]

DISCUSSION ON MODERN CONCEPTIONS OF INDUSTRIAL LUNG DISEASES

Dr. Charles L. Sutherland: In 1931, Professor E. L. Collis read a paper to the Section of Epidemiology of this Society entitled "Recent Views on Pneumoconioses" (*Proc. R. Soc. Med.*, 24, 531). I do not propose to bring this general review up to date, but this meeting of the Section of Radiology offers a suitable opportunity to discuss the role of radiography in the diseases due to dust inhalation, in industry.

As long ago as 1907 Summers of Bendigo, Australia, first pointed out the value of X-ray examination of the lungs in the diagnosis of pulmonary dust disease. Soon afterwards at the Rand gold mines in South Africa its extensive application to the diagnosis of miners' phthisis for the purposes of Workmen's Compensation established it on a very strong foundation. But this South African experience, while it is very extensive, is, at the same time, very restricted in that it relates to one particular occupation and the peculiar working conditions incidental thereto, viz. the underground drilling in the gold-bearing quartz. In this country, on the other hand, there are numerous occupations in which the workers are exposed to dust inhalation. Not only do these occupations differ from each other in the quality and quantity of the dust cloud, but in the same process or occupation there are equally wide variations at different working places and different working times. The physique of the individual workman is also a variable factor. It is therefore not advisable from the radiographic evidence alone to draw conclusions as to diagnosis and prognosis of the pneumoconioses; all the other evidence, especially the duration and intensity of the dust exposure, must have due consideration.

This is made very clear in the Annual Report for 1943 of the Senior Medical Inspector of Factories (Dr. Merewether): "Essential for the correct interpretation of many X-ray appearances which may be ascribed to the inhalation of industrial dusts (or fumes) is a very detailed knowledge of the processes which may be causative, of the character and amounts of the dust evolved, together with a most careful investigation of the work of each individual concerned since first he entered industry. This often requires a knowledge of the progress of and change in a particular process, since present disease may be due to antecedent conditions of work, long since remedied.

"Still more is this essential for determining the weight which should be attached to such abnormal appearances both as regards the outlook for the individual and the advice which should be given to him and in assessing the need for and nature of any preventive measures in the process. Admittedly, with the exception of silicosis and asbestosis, we are only touching the fringes of knowledge of the pneumoconioses. There is, however, already sufficient evidence that abnormal X-ray appearances which may be discovered in workers exposed to dust or fumes but which are not caused by non-occupational diseases, do not always signify any present or impending disturbance of health, still less should they be regarded as necessarily signifying the existence of a definite occupational disease. They may, and often do, indicate exposure to an industrial dust, but that does not necessarily imply the existence of a pneumoconiosis, or disease, or present or future disablement, any more than the discovery of asbestosis bodies in the sputum by itself determines anything but exposure to asbestos dust, and that not necessarily to a significant degree."

Dr. Merewether mentions two conditions, asbestosis and silicosis. Whilst asbestosis occurs amongst workers in a limited number of occupations manipulating asbestos, silicosis on the other hand is widespread because of the numerous occupations involving the handling or breaking of quartz, flint or stone which contain free silica SiO_2 in large proportion. The characteristic action of free silica in the lungs has been closely studied by workers in all parts of the world and definite conclusions reached as to its effects, if not as to its mode of action. There are, however, many industries which involve the risk of inhalation of mixed dusts containing silicates and small proportions of free silica. These mixed dusts produce effects which differ from those of free silica. There

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radiographically with some increase of the shadows—both dendritic and reticular—normally cast by the connective tissue of the lungs."

Significance of classical nodular silicosis.—When one has to deal with the individual workman who presents the radiographic picture just described two aspects have to be considered: in the first place, his ability to work, and, secondly, the prognosis. The radiograph, whilst it reveals to us that damage has been done to the respiratory capacity, does not tell us what reserve power the lungs possess. The clinical condition therefore is the chief factor in assessing the physical capacity of the worker. Very often the man is fit to carry on his present occupation but would find it difficult to take up a new one, yet he may be advised by his medical adviser to leave his occupation. This may be sound advice on the principle that the first object in treatment is to remove the cause of the disease. In this connexion Dr. Mercwether's point that present disease may be due to antecedent conditions of work, long since remedied, should be carefully noted.

Dominating the prognosis is the possibility of the presence of tuberculosis or its intervention later on. Every case of silicosis is potentially a case of tuberculosis; the film must therefore be carefully scrutinized for any indication of infection. Here too the clinical condition and history may be of profound importance. But while we know that 60 to 70% of those who die of silicosis have also tuberculosis, a great number of the sufferers from silicosis live on for years and carry on their work, to die ultimately of the ordinary illnesses of mankind. This is especially so in industries such as the potteries, where silicosis affects the advanced age-groups.

Pneumoconiosis of coal miners.—In the coal-mining industry there are a great many occupations where the workers are exposed to the inhalation of dust. There is a great variety of dust and mixtures of dusts in the different coal-fields, and the individual collier may be exposed to a different type of dust according to his place of work. Moreover the actual intensity of exposure has increased of late years owing to the more intensive methods of mining. The collier has become dust-disease conscious so that the radio-

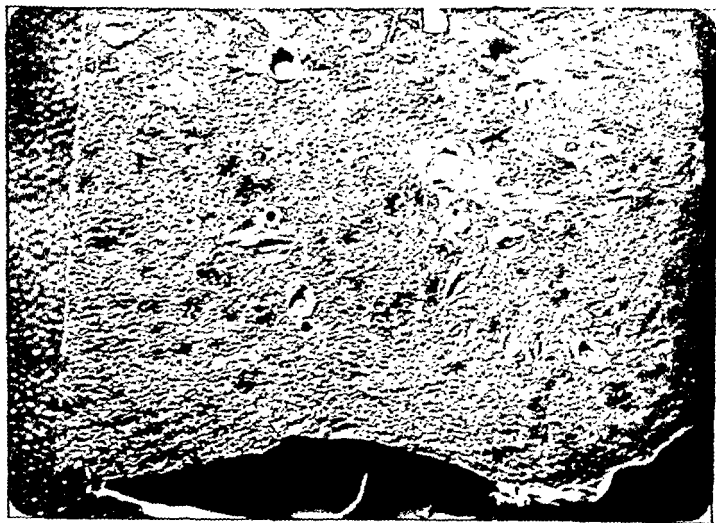


FIG. 1.—Dust reticulation in coal miner's lung.

logist in a coal-mining district is being asked to examine an increasing number of chests. The law has made the condition a compensatable one. A Special Scheme under the Workmen's Compensation Acts has been made providing compensation for coal miners in respect of disablement and death by pneumoconiosis and pneumoconiosis accompanied by tuberculosis. Pneumoconiosis in the Scheme (1943) is defined as "fibrosis due to silica dust or other dust and includes the condition of the lungs known as dust reticulation".

The lung conditions found in coal miners may be divided into three types: dust reticulation, nodulation, and massive fibrosis.

Reticulation is probably the effect of simple overwhelming of the defences of the lungs by dust of respirable size. The lymphatics become packed with dust cells and localized accumulations of dust and dust cells appear which have been called "coal nodules" by

has been a tendency to regard the action of such mixed dusts as merely silica effects modified by the presence or by the action of the other constituents. Certainly this point of view has allowed many cases of fibrosis of the lungs to come within the scope of the Workmen's Compensation Act, 1930, in this country, in which silicosis is defined as a fibrosis of the lungs due to silica dust. It is true that most dusts which have produced lung lesions have been shown to contain at least some percentage of silica so that it has been impossible either to acquit the silica or to condemn any other substance as the injurious agent.

Fibrosis Due to Free Silica

This is frequently given the convenient name of "classical silicosis" and it is found in such occupations as potter, stonemason, and metal grinder. Free silica produces a characteristic naked-eye and microscopic pathological lesion, the silicotic nodule, scattered unevenly throughout the lungs. When the lung is cut, the nodules stand out from the surface. The silicotic nodule may appear singly or form a larger mass by the fusion of several nodules. Each is composed of whorled collagenous connective tissue. It contains some dust in its interstices but more dust is found aggregated on the periphery of the nodule. The collagenous fibrosis seems excessive in relation to the amount of dust; as Belt (1939) has pointed out, silicotic fibrosis is a redundant fibrosis. Throughout the lung generally there is slight evidence of dust deposition; there may be some emphysema but this is not usually a prominent feature. There is some inflammatory thickening of the pleura especially at the apices.

These multiple nodules are the cause of the nodulation or "snowstorm" effect on the X-ray film. Each circumscribed spot is the shadow of a fibrotic nodule. Occasionally in old-standing cases the nodules become partly calcified, with a corresponding increase in the opacity. Sometimes, however, the fibrosis may have so contracted as to throw a shadow dense enough to suggest calcification. In the space between the nodules there may be a general haziness and evidence of emphysema, but no striation is ordinarily observed.

The formation of the fibrotic nodule represents to some extent a final result; it marks the encapsulation of the noxious silica dust. The nodular morphology is explained by King and Belt (1938) on the basis that the dust in the first instance tends, to collect in spherical foci. But radiographically, the appearance of nodulation gives us the first pathognomonic evidence of the disease. In most cases of classical silicosis in this country this takes fifteen to twenty years to develop. During these years the worker has been inhaling dust perhaps regularly or perhaps only at intervals. The defensive mechanisms of the respiratory system are sufficient to deal with most of the inhaled dust so that despite the burdens laid on these defences by colds, catarrhs, and even pneumonia, it takes many years of exposure to produce nodules sufficiently large or numerous or mature to be recognized on the film.

The South African Miners' Phthisis Medical Bureau (1935) recognizes radiographic signs in this prenodule stage in the form of "well-marked linear striation" or "increased arborization". In this country and in America the general opinion is that linear striation or general arborization cannot be regarded as specifically diagnostic of silicosis. If, as it is claimed, cases with such radiographic signs often show typical nodular fibrosis at autopsy, it can equally be said that silicotic nodules may be found without such radiographic signs. Cases in which an increased arborization is followed by definite silicotic nodulation are met with, but not consistently. But relying on a single X-ray examination of an individual with an industrial history of doubtful value, there is a risk, as one American radiologist (Sampson, 1937) points out, of diagnosing a "stage of imagination." Difficulty arises when we find shadows which may or may not be nodulation, particularly where there is present a suggestion of tuberculosis. A knowledge of the processes is of help here, since intensity of exposure, that is the amount of dust reaching the tissues of the lung, is the chief factor determining both the length of time required to produce the disease in a diagnosable stage and also the extent of the resulting fibrosis. In the sand-blasters working under the old unsatisfactory conditions the disease developed in two to eight years and frequently the first recognized untoward event was the development of open tuberculosis.

On the other hand as Mavrogordato (1926) pointed out, the lung may be "effectively occupied" by silica, that is, it may contain a sufficient quantity of silica to produce silicosis, without evidence of silicosis during life or of fibrosis at post-mortem examination. This potential or latent silicosis has been noted also by King and Belt (1938) in Northern Ontario miners but they do not mention the radiographic findings. Watkins-Pitchford (1927) in discussing the condition says that it presents no specific signs and cannot therefore be diagnosed with certainty during life. He goes on to say: "It is probably associated

ties of coal miners' pneumoconiosis led to more reliance than it deserved being laid on chemical analysis of lungs as a diagnostic method. It is misleading in many ways and L. U. Gardner's protest (1942) is worth heeding: "While in general the silicotic lung tends to contain more total silica than the non-silicotic one, there is no particular quantity over which most of the positive cases occur. The often quoted figure of 1% of dry lung tissue is of no diagnostic significance. The only logical basis of comparison is the free silica content of the silicotic tissue. For reasons stated the unsupported demonstration of silica in lung tissue is without diagnostic significance. Since both disability and increased susceptibility to tuberculosis are the results of alterations in anatomical structure, the diagnosis must remain on a morphological basis." The radiologist will learn little from a chemical analysis. A careful study of the morbid anatomy and of the histology is of greater value. Gloyne (1936) suggests that the normal looking parts of the lung often give conclusive evidence histologically.

Reaction to other dusts.—Examples of dusts containing no carbonaceous material but producing effects somewhat similar to those in coal miners are to be found in fireclay miners. In cases reported by Deaner (1941) an X-ray appearance similar to that of reticulation and to that of the cricket-ball mass was noted. The number of cases is small and the composition of the dust is that of a silicate with 30% free quartz and about 3% iron. A few cases of pneumoconiosis in workers in fullers' earth (Middleton, 1940) show a reticulation quite comparable with the colliers' lung, but no massive shadows. One case of death from pneumoconiosis due to exposure to fullers' earth dust for thirty-eight years has been reported (Campbell, A. H., and Gloyne, S. R., 1942). The reaction found was a soft patchy fibrosis mostly of reticular character, the collagenous deposition was less marked than in silicosis and the dust particles were 15 to 30 μ in length.

In contrast to the conditions just described no radiographic evidence of change was found as a result of two investigations into the effects of the inhalation of the dust of alumina. In an investigation at Kinlochleven (Sutherland, Meiklejohn and Price, 1937) excessive reticulation was found in a few cases, but this showed no relation to exposure to alumina and was therefore not due to the dust factor. A similar investigation at a duralumin works gave similar results (Hunter, Milton, Perry and Thompson, 1944). Although the amount of dust exposure in these cases is much less than in the coal mining, there is to be expected a slight reaction of the foreign body type.

Reaction to dusts containing definitely radio-opaque particles.—Dr. Fawcitt will deal with hematite workers. In electric-arc welders and silver finishers reticulation and nodulation have been demonstrated radiographically. Autopsies of such workers and also animal experiments (Harding, 1945) have demonstrated that these findings are due to the radio-opaque dusts. There is no fibrosis even of a reticular type and apparently no disablement. Boiler scalers also show reticulation and nodulation which may be due to iron dust in many cases but silicosis has been demonstrated in one fatal case. Steel dressers and fettlers are exposed to silica dust and to a varying amount of iron dust. In time they develop a severe silicosis; but some cases show a reticulation not unlike that of the arc welders. There is the possibility that this may be due to the ferrous dust and may merely indicate the possibility of silica inhalation and not a silicosis lesion. At the moment a good deal of effort is being made to avoid the use of silica in the moulding of steel and iron by substituting silicates (Dust in Steel Foundries, 1944). If any of the shadows found radiographically in steel fettlers are due to iron we will still expect to find these even although the chief danger, that is of silica, has been eliminated.

Reaction to dust of fibre or plate form.—The typical example in this class is that of asbestosis. Here owing to the size and shape of the particle there is damage to bronchi leading to dilatation, the pleura is thickened and adherent at the base and there is also an interstitial fibrosis accompanied by emphysema. Definite X-ray changes are described as a ground-glass appearance of the lung parenchyma with a fine stippling; but such changes usually occur when physical signs are even more definite. In the production of this stippling there is a possibility of the density of the shadows being increased by iron either from the fibre or deposited from the body fluids (asbestosis bodies).

Asbestosis is not produced in the same way as silicosis. The cause is not a chemical effect, since very finely ground asbestos dust does not produce any irritation when injected in animals. The size, 60 μ , and shape of the particles is probably the main cause of the characteristic changes.

In the preparation of this paper much assistance has been given by members of the Silicosis and Asbestosis Medical Board, by Dr. Merewether and Dr. Middleton of the Factory Department of the Ministry of Labour and National Service, by Dr. S. Deaner, Dr. S. R. Gloyne, Dr. H. E. Harding, and by the President of the Section, Dr. J. L. A. Groul, and this assistance is gratefully acknowledged.

Badham (1936 and 1939). Focal emphysema gives a honeycombed appearance to the cut surface.

Belt (1942), by using a special silver stain, showed that the dust-laden phagocytes in the localized accumulations were held together by fine reticulum fibres. These fibres are produced in just sufficient numbers to do this; there is no redundancy as in classical silicosis. He claims that the condition is a fibrosis although that term is usually reserved for collagenous fibrosis. It is also claimed, since the dust is composed of some quartz as well as silicates and coal, that the fibrosis is a silicotic one. But reticulation can be produced in eight years or less, a shorter period than that in which we expect to find classical silicosis.

But whether we call it a fibrosis or not, it is unlikely that the reticular fibres play much part in producing the X-ray picture of reticulation; certainly not the part the collagenous fibres play in producing the appearances of silicosis. According to Gough (1944) the X-ray picture is produced by the superimposition in depth of the coal nodules on a flat film. This of itself might not be sufficient, but there is a contrast effect due to the accompanying focal emphysema. The question of radio-opacity of some of the dust must not be forgotten.

The disability caused by reticulation is usually of the very slightest, in many cases it is difficult to make out any disability at all. Reticulation has been rather slightly referred to as "old colliers' lung" but even in old colliers the possibility of it being produced in a relatively short period in recent years must not be overlooked. Cummins (1936) and many others since have pointed out the importance of emphysema in causing dyspnoea in coal miners. The radiograph does not give us much assistance in assessing this except perhaps that serial films may show its development at the bases. In some of the younger coal miners there is a distinct tachycardia (Keating and Thomas, 1939) but this appears to be functional since so far it has not been related to any cardiac change or to the degree of reticulation.

Nodulation.—The pathological conditions which give rise to the nodulation are three in number.

First one meets with classical silicosis in pit sinkers, hard headers, crutters, branchers and stonemen, all of whom may have to drill in silica rock. Such workers, however, may drill in other strata so that we cannot say that all fall victims to classical silicosis. Secondly there is a mixed form of silicosis, the medusa-head type, where there is a collagenous fibrosis accompanied by dust deposition. A third form may be due to coal nodules of larger size than in reticulation.

The radiographic appearance seen varies from the classical snowstorm to the doubtful nodulation seen in reticulation. An interesting variation is that of very fine nodulation almost a stippling.

Nodulation may progress to massing: the type found in stone workers runs the ordinary course of classical silicosis.

Massive fibrosis in its advanced form presents usually one or two masses placed centrally in each lung, with large emphysematous bulke at the bases and sometimes also at the apices. On cutting these cricket-ball or sausage masses, either a glossy black surface is found or a ragged black surface similar to that found on a broken "briquette". Sometimes the whole interior has broken down into an oily black fluid. Massive fibrosis may be less in degree and be present in different parts of the lung. It may be accompanied by nodulation. Microscopically it is difficult to make out the structure owing to the amount of dust.

The cause of the formation of these masses has been variously ascribed to: (1) Blockage of lymphatics by silicosis followed by excessive deposition of dust in one area. (2) Coalescence of nodules: this is rare, we do not often find a marbling of the cut surface of the mass. (3) Infection, particularly tuberculosis either pre-existing or superimposed on dust fibrosis. The liquefaction of the contents of the interior of the mass is often considered a manifestation of tuberculosis but it is difficult to find the organism in these cases. (4) Irritation, either caused by the dust or by the dust along with some infection, the mass would thus arise *de novo* without a definite preceding stage.

Although one frequently finds colliers working regularly who show these masses, the prognosis on the whole is not good. Most of the deaths due to pneumoconiosis certified by the Silicosis Medical Board are in this stage. Tuberculosis may of course be found with reticulation, nodulation or massive fibrosis, but it is often difficult to prove.

The cause of the coal-miners' pneumoconiosis has still to be ascertained, but there is almost general acceptance of the view that silica plays a large part, although its action is modified by the other dusts. The silicates present are not yet acquitted entirely and the coal has been held responsible by some because trimmers who work only in coal suffer from the disease. But as Belt points out, coal contains silica and silicates, and trimmers' lungs contain no more coal than some colliers' lungs. In the past the peculiarity

ties of coal miners' pneumoconiosis led to more reliance than it deserved being laid on chemical analysis of lungs as a diagnostic method. It is misleading in many ways and L. U. Gardner's protest (1942) is worth heeding: "While in general the silicotic lung tends to contain more total silica than the non-silicotic one, there is no particular quantity over which most of the positive cases occur. The often quoted figure of 1% of dry lung tissue is of no diagnostic significance. The only logical basis of comparison is the free silica content of the silicotic tissue. For reasons stated the unsupported demonstration of silica in lung tissue is without diagnostic significance. Since both disability and increased susceptibility to tuberculosis are the results of alterations in anatomical structure, the diagnosis must remain on a morphological basis." The radiologist will learn little from a chemical analysis. A careful study of the morbid anatomy and of the histology is of greater value. Gloyne (1936) suggests that the normal looking parts of the lung often give conclusive evidence histologically.

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Reaction to dusts containing definitely radio-opaque particles.—Dr. Fawcitt will deal with hæmatite workers. In electric-arc welders and silver finishers reticulation and nodulation have been demonstrated radiographically. Autopsies of such workers and also animal experiments (Harding, 1945) have demonstrated that these findings are due to the radio-opaque dusts. There is no fibrosis even of a reticular type and apparently no disabement. Boiler scalers also show reticulation and nodulation which may be due to iron dust in many cases but silicosis has been demonstrated in one fatal case. Steel dressers and fettlers are exposed to silica dust and to a varying amount of iron dust. In time they develop a severe silicosis; but some cases show a reticulation not unlike that of the arc welders. There is the possibility that this may be due to the ferrous dust and may merely indicate the possibility of silica inhalation and not a silicosis lesion. At the moment a good deal of effort is being made to avoid the use of silica in the moulding of steel and iron by substituting silicates (Dust in Steel Foundries, 1944). If any of the shadows found radiographically in steel fettlers are due to iron we will still expect to find these even although the chief danger, that is of silica, has been eliminated.

Reaction to dust of fibre or plate form.—The typical example in this class is that of asbestosis. Here owing to the size and shape of the particle there is damage to bronchi leading to dilatation, the pleura is thickened and adherent at the base and there is also an interstitial fibrosis accompanied by emphysema. Definite X-ray changes are described as a ground-glass appearance of the lung parenchyma with a fine stippling; but such changes usually occur when physical signs are even more definite. In the production of this stippling there is a possibility of the density of the shadows being increased by iron either from the fibre or deposited from the body fluids (asbestosis bodies).

Asbestosis is not produced in the same way as silicosis. The cause is not a chemical effect, since very finely ground asbestos dust does not produce any irritation when injected in animals. The size, 60 μ , and shape of the particles is probably the main cause of the characteristic changes.

In the preparation of this paper much assistance has been given by members of the Silicosis and Asbestosis Medical Board, by Dr. Merewether and Dr. Middleton of the Factory Department of the Ministry of Labour and National Service, by Dr. S. Deaner, Dr. S. R. Gloyne, Dr. H. E. Harding, and by the President of the Section, Dr. J. L. A. Groult, and this assistance is gratefully acknowledged.

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Each radiologist views the subject from the type, or variety of cases, which occurs in his own neighbourhood; and whilst various industries give rise to a characteristic radiograph of the chest, there appears to be a definite series of phases through which the pneumoconiotic passes from initial infection, or invasion, to ultimate departure from this earthly sphere, be he stonemason, coal or iron-ore miner, or boiler-scaler, &c., but with subtle differences. The progress as shown in the radiographs is governed and varied by occupation and incidence of extraneous influences and infections.

I propose to show and describe a series of illustrations in one particular industry to exemplify a type and point out individual variations and some of the pitfalls in differential diagnosis. These are legion. The first pitfall must assuredly be traced to faulty radiographic technique; the ordinary standard P.A. chest radiograph should be taken in the first place and followed, when indicated, by films of varying K.V. and position, to demonstrate cavitation, or the texture at the bases of emphysematous lungs, for example. The chest measurement and general build of the patient must be considered and allowed for. There is no standard exposure—but there is a standard radiograph. The exposure is indicated by intelligent observation of the patient.

The upper and lower portions of the thorax may need a different radiological technique. The presence of the female breast shadows does not exclude the existence of "dust" disease. The onus of errors in diagnosis must not be entirely laid at the door of the radiologist. The request "X-ray chest, please!" is not good enough. Gough has rightly said that "it is understood that the X-ray picture of reticulation can be produced in the normal way by change in technique".

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Once again let it be stressed that the progress from one stage to another is a gradual one in some cases, and in some of my illustrations the occupational history and clinical course of the case belie the radiological appearances. Each particular stage has

its pitfalls in the matter of differential diagnosis. The radiological picture varies, as stated, to some extent according to the trade or occupation of the patients; but the basic chain of progress is generally there. Superadded infection, however, may change the radiological picture with alarming suddenness. As Dr. Sutherland has said, the period of dust exposure is an all-important factor in the occurrence of dust disease, but in the case of the radio-opaque dusts, such as hæmatite, evidence of occupation—not of necessity, disease—may occur very early in employment. Similarly "organic", as opposed to "inorganic" dust infection, may be dramatically sudden in onset, and the primary radiological evidence may be a bronchiolitis of the snowflake or snowstorm type.



FIG. 1



FIG. 7



FIG. 2



FIG. 3

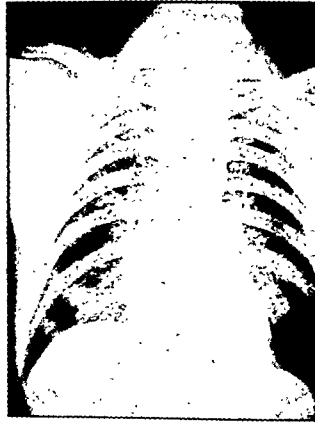


FIG. 4

[The author showed a series of radiographs of the chests of hæmatite iron-ore workers to illustrate the chain of progress of a type of pneumoconiosis.]

Hæmatite iron-ore exemplifies a *radio-opaque* dust. Its radio-opacity was demonstrated by Thurston Holland. More recently this has been emphasized by Craw, Fawcitt, Sander, Stewart and Faulds, and others. Various references to work on this subject may be found in a previous publication (Fawcitt, 1943). It is my opinion and that of other experienced workers in this subject that hæmatite iron-ore dust *per se* is innocuous in lung. Many of the following illustrations would appear to support the theory:

FIG. 1 demonstrates the opacity of hæmatite iron-ore in the clothing of a man who received severe crushing injuries. The hæmatite in the clothing occludes bone detail.

Stage of reticulation.—Radiologically, reticulation is evident as a fine network, of a lace-like pattern, sometimes sharp, but more often blurred in appearance. This network may occupy only part of a lung field, but more generally the whole of both lungs, the apices being comparatively clear—it is as pronounced in the outer fields and periphery as close to the hila. It may be seen associated with limited nodulation. Reticulation is to be differentiated from increased lung markings in that it demonstrates exaggeration of the pattern of the venous and arterial vessels in the lungs, the vertical or supporting structures of the arteries being more than usually evident and giving the lattice-work effect.

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The typical radiograph can be best described as snowflake mottling or snowstorm effect—and is seen in many dust infections—it is also seen in other than inorganic dust infections; it is seen associated with organic dust, as the result of bacterial or vegetable (mycotic) invasion.

The shadows produced by nodulation have an irregular and ill-defined margin and are discrete from one another—they are described as being 2 to 5 mm. in diameter. It is the next step beyond reticulation and accordingly is associated with it—its onset (true nodulation) is an insidiously progressive process. Some other observers do not accept this theory. The typical silicotic nodule is more opaque and of sharper definition, sometimes of varying density. The distribution is generalized as a rule.

It is only possible to demonstrate a few of these cases and illustrate some points of differentiation; but there is a marked difference in the behaviour and picture of the inorganic and organic dusts at this stage. Whereas the inorganic tends to progress from nodulation to coalescent nodulation, or, as in the (doubtfully) inert dusts when the source of danger is removed, become stable in appearance in the absence of superadded infection, the organic dust appears frequently to miss the stage of mottling of this type and progress to bronchiectasis of a massive variety, or, if the source of infection is removed, the appearance of nodulation may disappear.

As inorganic dust "disease" progresses, emphysema tends to increase, the vascular markings or so-called lung definition being lost in many cases in the lower zones; the hilar shadows become less evident and the excursion of the diaphragm diminishes, eventually to a very marked degree. Adhesions in the region of diaphragm are commonly seen; ruptured emphysematous bullæ may give rise to spontaneous pneumothorax. The heart is frequently narrow and displaced or rotated, and the borders blurred; particularly is this so in asbestosis. It has been observed by Amor that an increase in the hilar shadows with an associated tachycardia may indicate a mixed infection. Many men, however, develop the hypertrophic type of heart and eventually cardiac failure. These changes may be observed radioscopically.

Furthermore, if the patient be rotated into the oblique position, an enlarged tell-tale paratracheal gland or glands, likened in appearance to a short sausage, may be brought into view. This gland contains silica early in dust infections.

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FIG. 6.—A. G. Here is the typical mottling of hæmatite iron-ore. This is not due to silicosis, but to the particles of iron in the walls of blood-vessels and the interstices of the lung alveoli. This man died from malignant disease of the stomach.

FIG. 7 is a section from his lung—unstained—the typical red lung of the hæmatite iron-ore worker—the particles of iron are seen (see *Craw*, p. 30).

FIG. 8.—By way of contrast, the denser, more sharply defined nodulation of silicosis, also in a hæmatite iron-ore worker.

It is of note how very closely the radiological appearances in electric-arc welders (Sander, 1938 and 1944; Doig and McLaughlin, 1936) and boiler scalers (Dunner and Hermon, 1944) simulate the hæmatite iron-ore workers.

FIG. 9.—J. L. Farm worker infected by *penicillium* sp. occurring in mouldy grain, exhibits a softer type of mottling with emphysematous lung bases, mid-fields more general affected. The mottling is not so well defined towards the periphery. This particular case made a slow but ultimately complete recovery.

In military tubercle the nodular appearance is more discrete and evenly distributed throughout both lungs, the apices being equally affected. An atypical case may be very misleading.

FIG. 10.—Secondary carcinomatosis—the nodulation is usually much larger and considerably more discrete. There are other types, of course, where the nodulation is smaller.

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FIG. 12.—W. J. W., Furness miner, with little evidence of hæmatite, but evidence of the dense, hard mottling of silicosis of the South African miner (he spent many years on the Rand) and the coalescent mottling and cavitation of tubercle.

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Commencing reticulation is shown in:

FIG. 2.—T. W., aged 51. Fourteen years farm servant. Nineteen years in hæmatite iron-ore mines, the ore being oily and of low silica content. No pulmonary disability.

FIG. 3.—J. W., aged 62. A gunpowder worker, worked 40 years making black powder. In the process, charcoal, brimstone and saltpetre are employed and ground up to a powder in the mills—the powder is polished with blacklead. The reticulation seen in the radiograph is very pronounced and one wonders which of the four ingredients employed may be radio-opaque. He died at the age of 70 from pulmonary tuberculosis. No P.M. examination.



FIG. 5

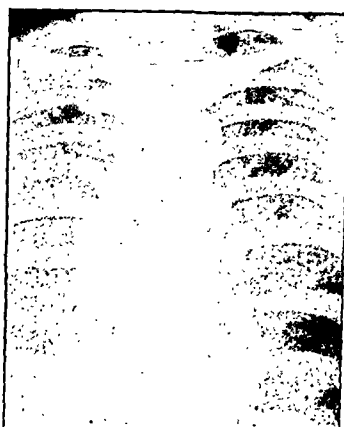


FIG. 6



FIG. 8



FIG. 9



FIG. 10

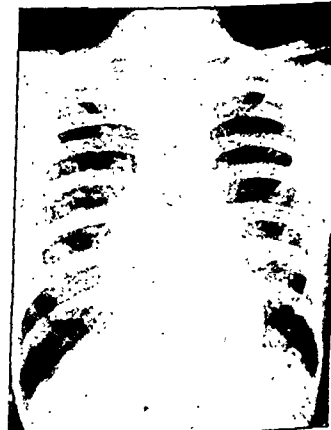


FIG. 11

FIG. 4 (J. B., aged 53) is illustrative of the permanency of the appearance of reticulation verging on snowflake mottling. Worked in iron-ore mines for seven years. On machines five months—since a County roadman for over thirty years. Very well. Chest expansion $3\frac{1}{2}$ in.

FIG. 5.—J. R., aged 56. Shot firer. Iron-ore labourer eight years. Shot firer thirty-two years in coal mines (reticulation). No machines. Some dyspnoea. The radio-opaque dust (iron) tends to monopolize the picture.

Stage of nodulation.—The so-called stage of nodulation—or in some trades of apparent nodulation—is in my opinion the villain of the piece as far as “confusion” in interpretation of the radiographs is concerned. The appearance may signify pathology or represent an apparently innocuous condition.

There is considerable variance of opinion, as to the sites of the initial development of nodules. To quote Twining—they are said to appear (1) “round the root of the lung on the right side” (Pancoast and Pendergrass); (2) “in the upper lung fields between the lung roots” (Entin, Klekmet, Kastle, cit. Assman); (3) “in the lateral mid-fields” (Krause and Loben); (4) “in the lateral middle regions”; (5) “in the lower lobe” (Staub Otiker). In Twining’s experience, mostly amongst stonemasons, nodules are seen early in the course of the disease at (1) the postero-lateral region of the upper lobe; (2) the apex of the lower lobe.

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FIG. 3.—J. W., aged 62. A gunpowder worker, worked 40 years making black powder. In the process, charcoal, brimstone and saltpetre are employed and ground up to a powder in the mills—the powder is polished with blacklead. The reticulation seen in the radiograph is very pronounced and one wonders which of the four ingredients employed may be radio-opaque. He died at the age of 70 from pulmonary tuberculosis. No P.M. examination.



FIG. 5

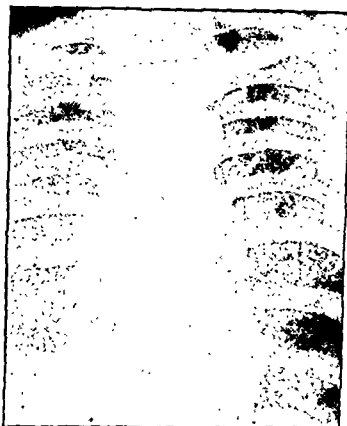


FIG. 6

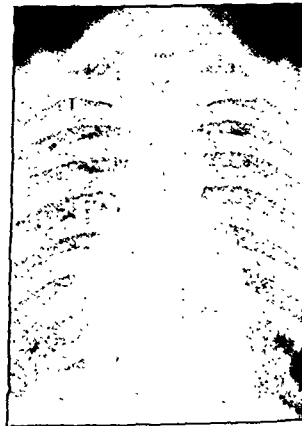


FIG. 8



FIG. 9



FIG. 10

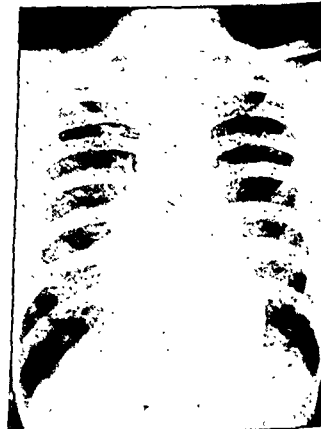


FIG. 11

FIG. 4 (J. B., aged 53) is illustrative of the permanency of the appearance of reticulation verging on snowflake mottling. Worked in iron-ore mines for seven years. On machines five months—since a County roadman for over thirty years. Very well. Chest expansion $3\frac{1}{2}$ in.

FIG. 5.—J. R., aged 56. Shot firer. Iron-ore labourer eight years. Shot firer thirty-two years in coal mines (reticulation). No machines. Some dyspnœa. The radio-opaque dust (iron) tends to monopolize the picture.

Stage of nodulation.—The so-called stage of nodulation—or in some trades of apparent nodulation—is in my opinion the villain of the piece as far as “confusion” in interpretation of the radiographs is concerned. The appearance may signify pathology or represent an apparently innocuous condition.

There is considerable variance of opinion, as to the sites of the initial development of nodules. To quote Twining—they are said to appear (1) “round the root of the lung on the right side” (Pancoast and Pendergrass); (2) “in the upper lung fields between the lung roots” (Entin, Klekmet, Kastle, cit. Assman); (3) “in the lateral mid-fields” (Krause and Loben); (4) “in the lateral middle regions”; (5) “in the lower lobe” (Staub Otiker). In Twining’s experience, mostly amongst stonecutters, nodules are seen early in the course of the disease at (1) the postero-lateral region of the upper lobe; (2) the apex of the lower lobe.

contain hæmatite or even possibly silica. Note reticulation is not seen in tomographs. Hydatid disease should not be confused with pneumoconiosis, nor should lymphadenoma. Malignant disease of lung is a more difficult proposition.

FIG. 16.—T. C. Dr. Sutherland considers this to be a massive fibrosis of the upper zone of right lung. The patient died. No P.M. was available. There is, of course, some evidence of fibrosis of left lung also and the collapse of a portion of right lower zone suggests possible carcinoma of a basic bronchus. Massive fibrosis may invade any lung zone, in which case superadded infection is usual.

FIG. 17.—T. H., aged 42. Iron-ore miner twenty-five years, and worked on stone-drifts. Illustrative of mixed infection. Note the coarser, denser nodulation, plus multiple massive fibrosis. T.B. positive.

The fluffy type is nearly always bilateral and frequently very extensive, and may invade any field and be confused with tubercle (and indeed most cases are T.B. positive) or bronchiectasis or even grosser secondary malignant disease—various mycoses give a very similar picture.

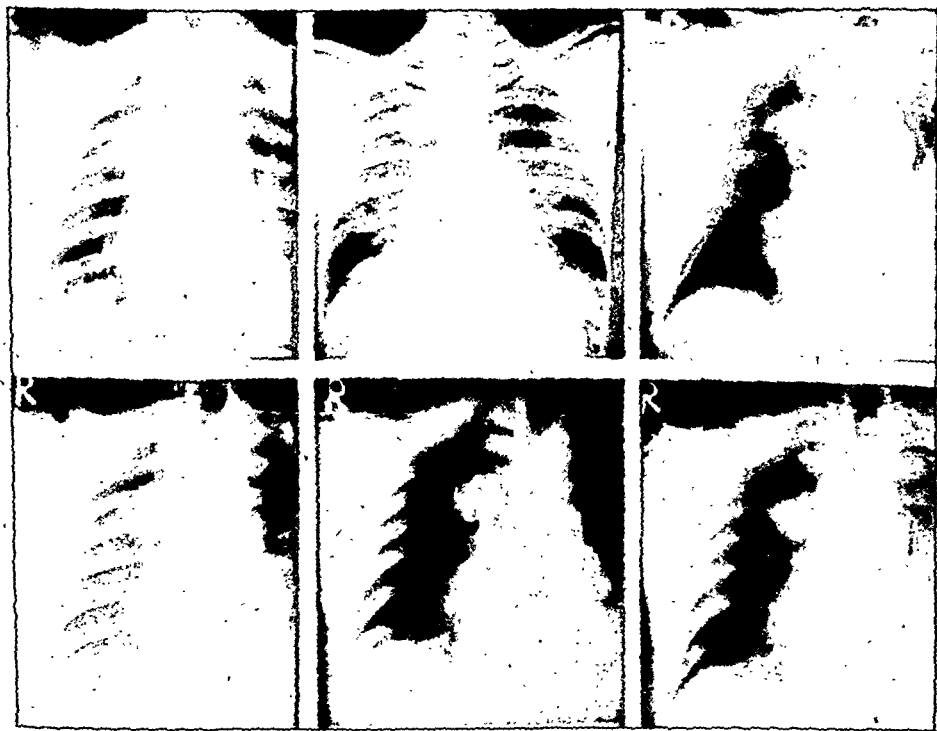


FIG. 15

FIG. 18.—J. J., is an advanced case of what has now achieved the popular title of farmer's lung (mouldy hay dust). The patient died. The radiological appearance is somewhat similar to fluffy type—and may easily be confused with actinomycosis or syphilis (see previous publication, Fawcitt, 1940).

Full history, clinical and pathological investigation are again stressed.

I conclude with three problem pictures:

FIG. 19.—L.A.C., R.A.F., aged 35, three years ten months in the Service—a keen rugger player—admitted to R.A.F. as A.I. He developed pneumonia in Italy which cleared up slowly and he was examined radiologically. Diagnosis—miliary tubercle—and he was sent home. Further X-ray examinations were made in this country. Patient now was diagnosed as silicosis and was discharged from the Service with no pension as he could not have contracted silicosis in the Service. I saw him in November—he had refereed a football match the previous day—his chest expansion was 3 in. He worked seven years in iron-ore mines. This is the mottling of hæmatite.

FIG. 20.—J. P., aged 61. Enjoyed good health in youth. At age of 17 he became a stonemason, working on free stone which is known to cause silicosis, later on limestone; which trade he followed for twenty-three years, but left because his health was affected and he had lost 21 lb. rather quickly. He had a chronic cough and was told in 1918 that his left lung was not functioning. He has since had many colds, attacks of influenza and bronchitis. 1918 to 1922 he was employed as a gamekeeper, and it is of note that the grouse on his moor died in large quantities in 1919 from some respiratory trouble. This may be a coincidence. The cause of the disease is not mentioned, but aspergillosis is common amongst birds. He gave up this work because of his shortness of breath on

Coalescent nodulation is self-descriptive. The nodules tend to become conglomerate or coalescent. Some earlier illustrations may demonstrate this to some degree.

Massive shadows.—*Multiple stuffy shadows* and *major consolidation* have been described under the single heading *consolidation*—with these may be included advanced coalescent nodulation—it merely defines a progressive process. The bugbear is, of course, as mentioned before, superadded infection. The massive shadows may be confined to one lung, to one zone; they may be small or resemble a cricket ball in appearance; the edges may be sharp or they may be indefinite. At this stage emphysema is almost invariably present.

FIG. 13.—J. C. (9.7.35) illustrates a lesion confined to the upper zone of right lung, the left lung not being above suspicion.

A film taken 1.6.42 showed healed tubercular disease of 9th and 10th dorsal vertebrae. This actually occurred since 9.7.35; but never has he had any productive cough nor a sputum positive to T.B., and yet the higher K.V. seemed to demonstrate a cavity in right lung.



FIG. 12



FIG. 13



FIG. 14

A further radiograph, 24.1.44, showed the lesion in right apex to be rather more massive. He does not work but has a measure of reasonably good health and still lures salmon from the River Eden.

FIG. 14.—By way of contrast, a case similar in appearance, W. M., referred to my department 13.12.34, at which time I suggested he might be suffering from sidero-tuberculosis. He was referred again 6.9.38, when by means of a film of high K.V. a cavity was demonstrated within the "mass" in the upper zone of his right lung. A cavity of this type contains much debris which resembles tomato juice in appearance. In this case tubercle bacilli were found in his sputum; in spite of this, he worked until the middle of 1939 and died in February 1940, having infected with tuberculosis five of his six children.

I have already stated that in my experience the distribution of these single shadows (massive) is most common in the central field of the upper zone of right lung in pneumoconiosis—any departure from this must suggest superadded infection as in the previous case, or tumour.

FIG. 15, which I shall describe in detail, is instructive. J. W., aged 48, iron-ore miner thirty-four years. Complaining of shortness of breath for three months. He had little cough and no sputum. A month previously he coughed up about an ounce of bright red blood—this gradually stopped, but was followed by vomiting. He had a cold at the time but no night sweats; pleurodynia was complained of about a month ago, pain radiating into the scapular areas. Chest expansion 3 in. Good for a miner. Little to be found by means of stethoscope. Sputum negative for tubercle.

19.5.42: The radiograph of chest shows the typical snowflake mottling associated with haematite iron-ore miners, together with the usual patchy areas of emphysema. Lying in relation to the shadow of the anterior end of second rib and in second interspace on right side is an opaque, rounded shadow which has a dense calcified wall, and lying to its outer aspect are two "daughter" shadows, if not three. The shadow does not appear to be typical of the "snowball" area of consolidation seen in these miners—and suggests osteochondroma of rib; screening in lateral plane, however, excluded this. Hydatid disease was suggested—the tests for hydatid were ultimately carried out and proved to be negative.

15.6.42: A series of tomographs seem to indicate chondroma of lung, an opinion expressed by Morrison Davies. Tomographs were taken at the depths of 3, 5, 6, 8 and 11 cm. from the posterior skin surface, the patient being in the supine position. The mass already described in the upper portion of the right chest comes into definite view at 6 cm. It is seen to be of varying density, to have a calcareous rim and to be lobulated. The tomographs also show that the hilar and peri-hilar glands are dense and probably

the fringe of this enormous subject. For example, I have not dealt with bagassosis (sugar-cane dust) as described by Castleden and Hamilton-Paterson, nor have I dealt with the effects of noxious gases on previously healthy lungs, nor the effect of noxious gases on lungs already containing metallic dust particles.

Concerning the influence of rotting timber in mines. Are the micro-fungi therein deterrents or adjuvants in the incidence of pulmonary disease? I am now inclined to the former theory. These are just a few examples of the new and additional difficulties which must confront radiology since this subject of "The Industrial Lung" was dealt with fairly exhaustively at the Annual Congress of the British Institute of Radiology in December 1937.

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FIG. 16



FIG. 17



FIG. 18



FIG. 19



FIG. 20



FIG. 21

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FIG. 3.—Perivascular dust accumulation. (Ocular $\times 6$ 16 mm. objective.)



FIG. 5.—Reticulin fibres ($\times 350$).



FIG. 4.— $\times 8$.
Microscopic Section.



FIG. 6.—Coarse nodulation.
Part of lung. Reduced (see Radiograph, fig. 8, Dr. Fawcitt).



FIG. 7.—Marginal field of a haemate nodule after Wilder's reticulin stain. Dense reticulation is easily seen. In the centre of the nodule there is evidence of miniature collagen formation.

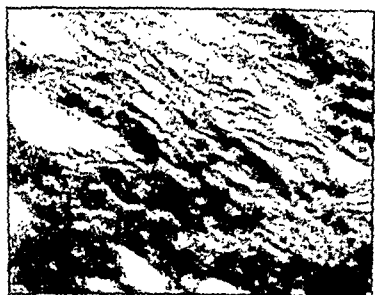


FIG. 8.—Marginal reticulation.



FIG. 9.—Fine nodulation. Contact print.

Fig. 3 shows first a nodule with ordinary staining (A). The second (B) is the same section after micro-incineration, with dark-ground illumination, and it should be noted that this section does not reveal any more particulate matter.

These slides show that almost the entire structure is particulate hæmatite and silica.

CHEMICAL ANALYSIS OF LUNG.

% Silica to lung 0.95	% Fe_2O_3 to lung 7.7
% Silica to ash 6.3	% Fe_2O_3 to ash 50
Total silica 2.35 grammes.	

(b.) *Lace Markings*: This type of X-ray reticulation is rare, and I have seen only two at post-mortem. Figs. 6 and 7 of Dr. Fawcitt's paper illustrate such a case. Again the cut surface shows no visible or palpable nodulation or other fibrosis and an ordinary

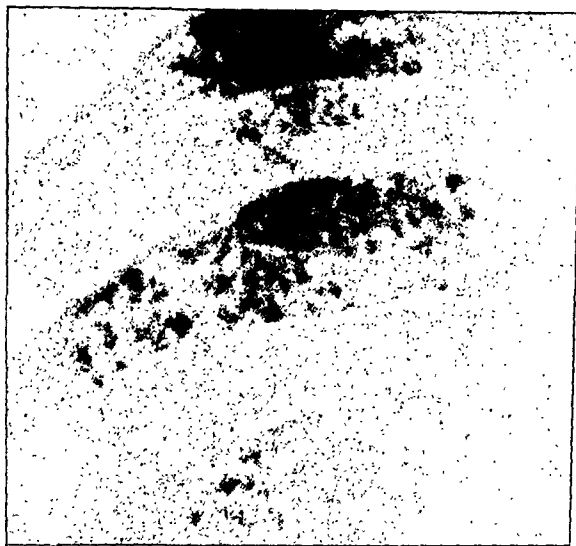


FIG. 1.—Reticulation. Contact print.



FIG. 2.— $\times 15$. Microscopic Section.

microscopic section ($\times 8$) shown in fig. 4 demonstrates the linear arrangement of the dust with concentrated deposits. It shows a pulmonary atrium and, just at the bifurcation, when stained with Wilder's reticulin stain, it shows very definite and fairly dense reticulation (fig. 5). The silica and iron content of such a lung is very high, in fact, almost the highest in the entire series.

CHEMICAL ANALYSIS OF LUNG.

% Silica to lung 1.0	% Fe_2O_3 to lung 12
% Silica to ash 8	% Fe_2O_3 to ash 49
Total silica 4.8 grammes.	

(3) *X-ray nodulation*.—Nodulation of a size of about 2 mm. is relatively uncommon when there are no associated conglomerate masses. A certain number do occur, and they are always in association with X-ray reticulation. Radiologically the nodules are without clear-cut edges, and the consistence of the shadow varies within the nodule. The cut surface of the lung is characteristic. The lung substance is either normal or very slightly brown-stained, and dotted over the surface are areas of brownish or reddish-brown nodules. They look and feel slightly raised above the surface and are slightly more resistant to touch than the intervening lung tissue (fig. 6).

Fig. 7 shows a nodule stained with hæmatoxylin eosin. The same nodule incinerated revealed much fine particulate material, and, after HCl digestion, much insoluble residuc. Fig. 8 is a marginal field of this nodule after Wilder's reticulin stain. Dense reticulin is easily seen. In the centre of the nodule there is evidence of immature collagen formation.

CHEMICAL ANALYSIS OF LUNG.

% Silica to lung 1.03	% Fe_2O_3 to lung 6.56
% Silica to ash 7.2	% Fe_2O_3 to ash 46

I have seen only one post-mortem case showing mature collagenous nodulation without massive shadows, and this conforms to the X-ray type of fine nodulation. Fig. 9 is a contact print from such a case.

Cut section of the lung showed no fibrosis to the naked eye.

Section of Laryngology

President—C. GILL-CAREY, F.R.C.S.Ed.

[March 2, 1945]

DISCUSSION ON AN UPPER RESPIRATORY CLINIC FOR CHILDREN

The Willesden General Hospital, London

F. C. W. Capps: The routine examination of children with nasopharyngeal symptoms is apt to become a matter of habit in clinics strictly confined to their own particular field.

To deal with this, a team seemed to be indicated: (a) To interpret history and symptoms in terms medical and social, (b) to encourage repeated attendances in order to avoid a hurried decision at a single consultation, to record progress, and to maintain the physiological response to environmental infection, free of symptoms; (c) to investigate the devolution of the mouth-breather and to combine the resources of the speech therapist, rhinologist and orthodontist, to reverse the process; (d) to deal with nasal and bronchial catarrh as a single pathological entity with the nasal cavities and accessory sinuses as the upper, and the bronchial system as the lower bacterial barrier; (e) to employ routine radiography of the sinuses with the object of early recognition and clearance of occluded areas and soft tissue radiography to show the presence of a pad of adenoids; (f) to recognize and remove tonsils that are subject to recurrent bacterial invasion and inflammatory reaction, particularly where morbid changes may have taken place which threaten the lymphoid barrier.

In the child it should be possible to correct disturbances before an established pathological state supervenes. It is not easy to keep this viewpoint when one is seeing children in a general clinic. An E.N.T. Clinic for children only was therefore started.

The team at present consists of a social worker, rhinologist, speech therapist and orthodontist. Children are seen by members in this order, but not necessarily on the same day. We should also have a paediatrician and he may be the controlling member.

The persistent mouth-breather has been our especial concern. The association of a rhinologist and orthodontist to investigate this condition is not new, for Warwick James and Somerville Hastings read a paper on "Mouth Breathing and Nasal Obstruction" to the Section of Odontology in 1932. (*Proceedings* 25, 1343.)

During childhood the sinuses are not fully developed, and the pharyngeal lymphoid tissue undergoes physiological hypertrophy.

It is of interest to note that at puberty when the sinuses reach a stage of development comparable with that of the adult, the phase of lymphoid hyperplasia is replaced by a process of atrophy; if the tonsils and adenoids are removed at an age when the sinuses are immature, a generalized hyperplasia of the pharyngeal lymphoid tissue may follow.

Fig. 10 is a micro-section. The nodules are seen to be discrete, averaging 1 mm. or less in size and mostly of irregular shape. It shows the variation in size and shape of the nodules, and they resemble the types described by Belt. The nodules are much smaller than the previously described type of nodulation.

Fig. 11 shows a nodule which in structure nearly approaches the classical type. One of the few I have found that was not associated with tubercle or other massive fibrosis. Ordinary staining shows concentric layers of collagen much more mature in the centre. With dark-ground illumination the refractive material was scanty, but after incinerating there was seen to be a very large amount of particulate matter, and after HCl digestion the silica pattern was seen to be arranged concentrically and less in amount in the centre. It is interesting to note that this nodule was subpleural, and, if a diligent search is made in cases showing no evidence of reticulin fibres in the dust nodules from the centre of the lung, an occasional nodule may be found 1/10 mm. in size showing primitive attempts at laying down of immature collagenous fibres.

This type of nodule, when stained with hæmatoxylin and van Gieson, shows definite fibrous tissue with fine markings in the centre, and, when viewed with dark-ground illumination, shows much less particulate matter, as it has been obscured by fibrous

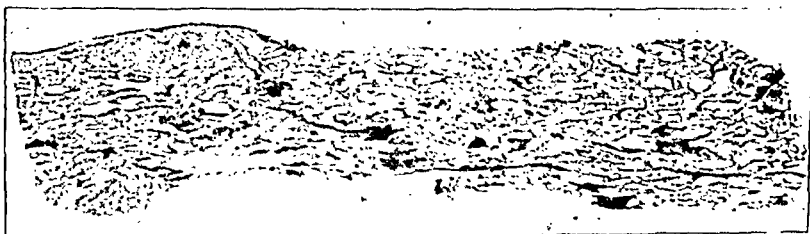


FIG. 10.—Fine nodulation. $\times 20$.

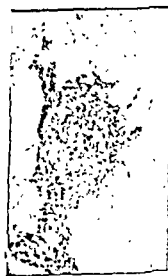


FIG. 11.—Nodule (classical type). (Ocular $\times 6$, 16 mm. objective.)

tissue. When incinerated there is shown much fine particulate matter, and finally, when digested with HCl, the pattern of silica is shown. The appearance simulating the classical nodule. Nodules such as these are always subpleural in location and very small. The nodules which are situated deep in the lung are of a typical type seen in previous type of nodulation.

CHEMICAL ANALYSIS OF LUNG.

% Silica to lung 0.89	% Fe_2O_3 to lung 7.84
% Silica to ash 5	% Fe_2O_3 to ash 44

CONCLUSIONS

(1) X-ray reticulation of hæmatite iron-ore miners shows as a very dense radiological shadow, which is due to the simple accumulation of particulate hæmatite. Pathologically there is no stimulation of collagenous fibrosis and practically no increase in the amount of reticulin fibres.

(2) Nodulation without massive fibrosis is a rare condition. The large type shows mostly tight packing of dust in perivascular locations, with moderate collagen formation, and the small type shows a percentage of the nodules to be very similar to the classical type.

(3) Large-sized classical nodulation only occurs in the presence of established tuberculosis and is always associated with solid fibrotic masses.

(4) The fibrotic response in the lungs bears no relationship to the total amount of silica or hæmatite present in the lung tissues.

I desire to record my sincere thanks to Dr. J. S. Faulds, Pathologist to Carlisle Infirmary, who has supplied me with the results of the chemical analysis of the lungs, and has helped me much in this work.

Dr. F. H. Kemp gave a brief account of an investigation which had been carried out with Mr. K. J. Cook and Dr. D. C. Wilson into the risk of pulmonary injury in boiler cleaning at one of the great railway depots. They had examined nine workers who had been employed whole-time in cleaning boilers at this works. Eight of these men considered themselves healthy but one complained of indigestion and breathlessness on exertion. The radiographs showed no significant changes in any of these cases. Dr. Kemp said that they had concluded that the changes which have been described by other workers may have been due to different methods which are practised in other works or that there were significant differences in the physicochemical constitution of the scale and flue dust.

A full account of this work will be published shortly

Soft tissue profile radiographs. (Mouth open.
The habitual co-ordinating of the palato-lingual musculature free of conscious control.
1. In the presence, 2. In the absence of adequate levels of tone and neuro-muscular activity.



FIG. 1.—An active palato-lingual reflex closes the faucal isthmus and preserves nasal breathing.



FIG. 2.—Failure of the palato-lingual reflex to close the faucal isthmus results in mouth-breathing.

Tracing of a soft tissue profile radiograph.
(Partly diagrammatic.)

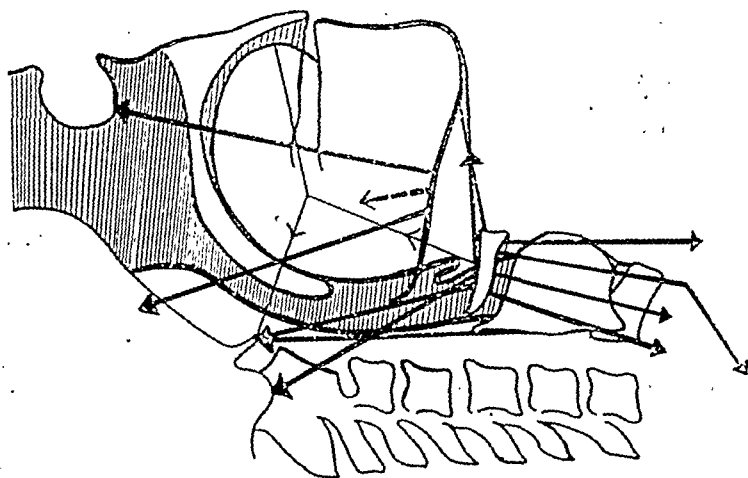


FIG. 3.—The holding muscles of the skeletal framework in relation to the airway. Reciprocal opponents in a state of balanced equilibrium, i.e. the position of physiological rest.

Routine serial radiography has proved to be essential in the correct interpretation of symptoms referable to the upper respiratory tract. Thickened or cedematous mucosal linings (56% in summer and 65% in winter over a series of 360 cases recorded in 1942-43) were rarely followed by infected antra. Surgical treatment was not indicated.

The high incidence and transient nature of sinus opacities suggest that the lining mucosa shares in the defensive reactions of the upper respiratory tract, but the precise relationship with the inflammatory reactions of the lymphoid tissue is uncertain.

Our aim in treatment throughout should be to temporize until stability is reached.

Lack of aeration and occluded ostia are the precursors of impaired ciliary drainage and retention of secretions. Proof puncture and aspiration, followed by repeat puncture and irrigation or ephedrine displacement, is employed in selected cases and progress controlled by serial radiography.

Exclusion of an established upper respiratory infection is essential before interference with the lymphoid barrier is contemplated.

In discussion of the tonsil problem here in 1940 (*Proceedings* 33, 347), repeated attacks of inflammation received priority and were held by some to be the only indication for operation. The observation of Kershaw at that discussion is worth repeating—"that operation during the stage of physiological response to environment is contra-indicated".

An investigation made in 1931 suggests that a deficiency in the diet of fat-soluble vitamins is one of the factors, though not predominant, which tends to produce an overgrowth of adenoid tissue. Increased knowledge of causation and prevention can only come from a more thorough medico-social investigation of the first three or four post-natal years and maternal history during pregnancy.

In 1943 there were 557 new cases and attendances for progress numbered 2,400. Tonsils and adenoids were removed from 216, that is 48%. For 1944 the new cases were 440, attendances for progress 2,200, operation for tonsils and adenoids 158, or 36%.

We do not advocate that the clinic be copied until it can be shown to produce results superior to those already attained by the older methods of isolated consultant clinics.

E. Gwynne-Evans: The mouth-breather problem.—The respiratory function requires the co-ordination of many muscles. Co-ordinated movement is an interplay between reciprocal muscles in alternating contraction and relaxation—two opposite physiological actions of muscle activity.

Although there can be no absolute state of muscle rest owing to tonus, the position of physiological rest corresponds to the normal position of equilibrium between antagonists.

A colour film was made demonstrating the reciprocal co-ordination of the tongue with the palatal velum in closure of the faucial isthmus.

These observations were supported by a large number of soft tissue radiographs of the palato-lingual musculature at physiological rest.

Serial radiographs have demonstrated the stability of the palato-lingual patterns, when care has been taken to ensure that the musculature has assumed the habitual position of rest before exposure is made.

The radiological pattern depends on the degree of tone and the habitual co-ordination of the musculature. Normally, if the mouth is open, the shadow of the palatal velum is contracted round the base of the tongue, which is elevated and retracted to close the palato-lingual space.

When the musculature is unduly relaxed, the jaws are open, but the arching of the tongue is inadequate, and the palatal velum occupies a midway position between the post-nasal and palato-lingual spaces.

In the presence of an obstructive pad of adenoids, the jaws are usually open, and the co-ordination of the musculature is disturbed. The adenoid shadow may obliterate the post-nasal space, the posterior mass of the tongue is depressed away from the palatal velum, whilst the tip of the tongue may impinge against the pre-maxilla.

These are the two distinct patterns of the established mouth-breather; the pattern of the intermittent mouth-breather may be indeterminate.

Negus has shown that keen-scented mammals are provided with an elongated palate which is in contact with an efficient epiglottis to preserve the olfactory sense with the mouth open. He has pointed out that with "... the recession of the jaws and the

Enlarged tonsils or adenoids interfere more directly with velar action and the drainage mechanism. On the other hand; the constant repetition of oral breathing as the result of an inability to overcome persistent post-nasal obstruction will produce a wrong habitual co-ordination of the palato-lingual musculature which may or may not continue after the cause of the obstruction has been removed.

The Orthodontist has related failure of the *orbicularis oris* and *alae nasi* in some cases to a state of imbalance among the facial muscles associated with a malrelationship between the jaws.

Methods of investigation.—Children are examined jointly by the rhinologist, speech therapist and orthodontist. The upper and lower respiratory mechanisms are grouped together as reciprocal antagonists and considered in terms of neuromuscular activity under the growing influence of cortical control. Clinical estimation of function is supported by radiography. A profile radiograph of the palato-lingual musculature is exposed in the habitual position of rest during quiet respiration, and the costodiaphragmatic rhythm is observed under the fluorescent screen. While it is usual to relate the respiratory musculature to the postural balance of the body segments, the Orthodontist has taken a new departure by relating the upper respiratory musculature to the craniomandibular and cervical segments.

Management of cases.—Early recognition and clearance of occluded airways is an essential requirement whilst tonsils or adenoids that interfere with velar action are removed. It has become increasingly evident, however, that management of the habitual mouth-breather implies not only re-education of the anterior oral musculature, but the cultivation of tonus and reflex neuromuscular activity in the posterior groups of muscles that are responsible for ventilation and drainage of the nasal spaces.

Anterior oral musculature.—The plan of rehabilitation is considered from the myogenic aspect that "the position of rest is the physiological basis for re-education of muscle function" (Colin Mackenzie) and from the neurogenic aspect, by bringing muscle action into the conscious plane through games, exercises and devices that are designed to cultivate tonus, and by blazing a pathway through the synapses, encourage reflex muscle activity free of conscious effort, until correct habits of co-ordination are finally formed.

The Orthodontist's observations on the developmental pattern of the jaws in relation to the behaviour of the facial musculature and nasal respiration led us to adopt his method of using a modified Andresen appliance as an intra-oral splint to obtain an optimum relationship between the jaws and a state of balanced equilibrium between the muscles.

Re-education is begun as the *orbicularis oris* and attendant muscles of facial expression are actively moulded round the renewed basic support, and the previous unconscious behaviour patterns are upset.

Reflex tonus of the musculature is cultivated through the conscious effort necessary to hold the appliance in place at intervals during the day. Later, the splint may be retained without further thought or attention as a habit, and can be worn mostly at night.

Re-training of the anterior groups of oral muscles in correct habits of co-ordination involves neuromuscular pathways that are inter-related with the development of speech, and it may be desirable to pass cases through the hands of the speech therapists for special exercises before adequate kinæsthetic control is regained. An inability to combine the association of muscles at the necessary speed required for speech may call for a prolonged course of speech therapy.

Posterior oral musculature.—We regard the palato-lingual and palato-pharyngeal mechanisms as reciprocal antagonists that are not entirely under direct control; but are largely ruled through lower levels of the nervous system. The cultivation of tonus and reflex neuromuscular activity in the posterior groups of muscles are therefore not so dependent on bringing muscle action into the conscious plane. The Orthodontist has observed that recurrent acts of swallowing are induced by the presence of the appliance in the oral cavity and they probably play a large part in "re-conditioning" the posterior oral reflexes.

Comments.—There are indications that recovery of function follows the evolutionary sequence. Radiological evidence of palato-lingual closure has been persistently obtained, but tonic of the facial muscles and the reflex closure of the *orbicularis oris* free of conscious effort have been more difficult to achieve.

Where post-nasal obstruction has led to a wrong co-ordination of the musculature and

flexion of the head on the vertebral column; the larynx has descended in the neck, being forced to do so by the tongue, which assumes an arched shape. The result is the separation of larynx from nasopharynx with a wide gap between epiglottis and soft palate . . . ". We have repeatedly observed that an open mouth is not necessarily indicative of mouth-breathing but the palatal velum forms a tense low arch meeting the posterior mass of the tongue which is instinctively drawn upwards and backwards to close off the oral cavity from the airway.

Whilst we partly agree with Somerville Hastings and Warwick James that the reciprocal co-ordination of the tongue with the palatal velum constitutes a posterior oral sphincter, we suggest that the palato-lingual mechanism is basically a postural reflex, comparable to the reflex action of the glottis, and is a valve which is closed to preserve the function of nasal respiration if the mouth is open.

The reflex rhythm of the lower respiratory musculature is modified by the development of the cortex, but remains essentially automatic, and is less vulnerable than the evolutionary younger upper respiratory musculature which comes largely under the influence of cortical control. As the child learns to master his muscle activities they become a reflex practice, and the higher level control is replaced by a lower level mechanism with the development of muscle sense. Until the stage of stability is reached, the facial, lingual and palatal musculature is particularly prone to disturbances of co-ordination.

The most serious cause of muscle disturbance is loss of tone. Although any number of factors may produce the picture of the hypotonic child, tonus is basically a neurogenic property of muscle activity in which both higher and lower centres are concerned. The role of the higher centres is uncertain, but the frequent association of a dull mental attitude as a primary rather than a secondary factor should not be overlooked.

In the opinion of Sir Arthur Keith and G. G. Campion, the "narrow deeply arched palate, the so-called 'adenoid facies', is not a single defect in an otherwise well-developed face, but part of the failure in the general growth of the face".

We suggest that persistent mouth-breathing also, is not necessarily a single defect secondary to post-nasal obstruction in an otherwise healthy child, but may be part of the general failure in the proper development of neuromuscular activity. When combined with a dull mental attitude, habitual mouth-breathing might then be characterized as a true functional disorder.

An attempt has been made to analyse disturbances in terms of functional "disolution", an expression used by Hughlings Jackson as meaning the "reverse of evolution"; it is a method of approach that has already been adapted to speech pathology by Leopold Stein.

The preponderant holding muscles of the mandible are the masseter and temporalis. The mechanism in closure of the jaws is stronger than the mechanism of opening, so that when the musculature is normally relaxed, the mandible assumes a balanced position in light occlusion with the maxilla, known as the resting bite.

Failure of muscles follows a devolutionary sequence, affecting some, but not necessarily all, of their functions. Undue relaxation of the musculature allows the mandible to be released at any age; in older children, flaccid muscles of facial expression and certain speech defects including some deviations of nasality indicative of palatal disturbances are among the earlier signs. Mouth-breathing supervenes when the framework of the palato-lingual pattern is also relaxed, with a diminished or absent reflex to effect closure of the faucial isthmus when the mouth is open.

Stagnation of nasopharyngeal secretions may result from the added failure of the palato-pharyngeal musculature, to effect proper drainage of the post-nasal space.

Functional weakness is distinct from an organic paresis that would result in regurgitation of fluids through the nose. Negus points out that the swallowing movement commences in the highest part of the nasopharynx with the " . . . raising of the soft palate and closure of the nasopharyngeal isthmus by approximation of all its walls; initial closure is followed by a wave of constriction effected by the superior constrictor muscles with the object of squeezing out mucus, debris and bacteria dumped by the ciliary streams of the nose and sinuses, to be carried downwards through the pharynx into the œsophagus and stomach". When secretions are allowed to remain in contact with the pharyngeal wall for any length of time a subsequent lack of sensitivity to initiate the swallowing reflex increases the liability for nasopharyngeal infection to follow the alternative physiological route into the tracheo-bronchial system.

Thus, the most important clinical factor connected with the syndrome described in the opening paragraph is the position of the tongue in the oral cavity.

In the normal individual the integration of the structural units connected with mastication, deglutition and respiration produces a state of equilibrium—with the mandible and hyoid bone as a combined pivot or fulcrum.

In action a gentle synergic wave of contraction includes the temporal, the masseter, orbicularis oris and hyoid group, ending in a quick, uninterrupted, effortless act of deglutition, followed by relaxation. When the jaws are wrongly apposed medially, anteroposteriorly or vertically, this indispensable fulcrum is out of true and all the structural units connected with mastication, deglutition and respiration are compelled to act by adaptation.

Under favourable or normal conditions we have a distinct pattern of deglutition behaviour easily observed clinically, just as a normal gait has a definite pattern or character. Therefore only a correct anatomical relationship of the units concerned will permit free or physiological function of mastication and deglutition.

To correct faults the bony framework must be so reconstituted that the bimaxillary space provides ample room for the physiological requirements of the tongue, thus correctly positioning the larynx with the nasopharyngeal space.

The achievement of this ideal integration of structural units is an orthopaedic problem of some complexity and I would define this new approach as "cervico-facial orthopaedics".

After the jaws have been orientated in accordance with the above physiological requirements an improved Andresen type of splint is used for intermittent wear (mostly at night). Such craniomandibular intermittent immobilization with the corrected orientation allows the musculature to develop and the osseous structures to maintain their corrected position. The jaws being apposed by the splint are provided with the necessary fulcrum for the musculature during each act of swallowing and keep the airway in normal function from the moment the splint is worn. Fortunately, muscles being very readily trained, the splint provides the necessary stimulus for remoulding of the skeletal framework in response to the newly imposed muscular stresses, in accordance with the well-known principles of bony reconstruction as propounded by John Hunter, Wolf and others—frequently alluded to as "Wolf's law".

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Joan H. Van Thal: The aim is to restore function by getting the patient to perform actions already within his scope, based on innate patterns, though these patterns may be dormant. Fatigue and boredom must be avoided, and unnecessary effort or inappropriate responses eliminated.

For the young patient the approach is largely through games that give him the mental picture on which to base his respiratory behaviour; activity starts from relaxation and is not superimposed on musculature that is already fatigued. The games and exercises bring respiration into the conscious plane, i.e. under cortical control; thus correction and adjustment can be achieved, until a habit is formed, or, in other words, a conditioned reflex established.

In some cases inhalational therapy has been combined with breathing exercises. The

large tonsils have interfered with velar action, palato-lingual closure has also been obtained following operation in some, but not all cases.

General considerations.—Failure to maintain proper extension of the vertebral column plays an important part in the respiratory disturbances of the mouth-breather. Exercises and games which draw the child's attention to those groups of muscles that are involved in the general extensor reflex are combined with methods that encourage correct reflex habits of breathing.

A paediatrician is to be appointed to assess environmental, nutritional and metabolic factors that contribute towards hypotonus. The advice of a child psychologist is also required to determine intelligence levels and psycho-emotional factors before we are justified in suggesting that persistent mouth-breathing in the presence of a dull mental attitude may be a true functional disorder.

We have yet to judge the practical value of these methods of approach before they can be accepted as part of the routine procedure in the E.N.T. Department.

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Arnold A. Nove: I have observed that children with malrelated jaws and malposed teeth have not only facial asymmetry but tend to develop a stooping posture and winged scapulae. These are associated with post-nasal catarrh and other respiratory symptoms.

Close analysis will reveal this as a state of imbalance between intrinsic and extrinsic musculature of the head and neck.

Small dental arches and short or obtuse ascending rami prevent the tongue from occupying its proper position in the oral cavity. Instead of lying horizontally with its tip



FIG. 1.—The low level of the hyoid related to relaxation of the lingual musculature.



FIG. 2.—Same case after 10 months' treatment. Increased tonus of the musculature. Note relative positions of hyoid bone.

touching the lingual surfaces of the anterior teeth, the tip of the tongue abuts against the palate (behind the pre-maxilla). This causes the tongue and hyoid to sag, involving other closely related anatomical structural units connected with deglutition and respiration. This muscular imbalance, with consequent sagging of the tongue, is associated with facial disharmony as well as postural defects (see figs. 1 and 2).

no mention was made of the type of patient with what he might call the short upper lip. They had heard nothing at all about the importance of the use of the lips as a factor in moulding the shape of the jaws and mouth in addition to the splinting apparatus.

He understood Miss Van Thal to say that it was not practicable to do anything in the way of breathing exercises with children under 6. With this he disagreed. Miss Van Thal had also said that it was important that the child itself should observe if it was opening its lips during breathing exercises. His own feeling was that the most important thing was that the child should close its lips unconsciously, not consciously, and there was a simple way of making the child do that, namely by the holding of something in the lips. His own practice had been to make children do breathing exercises for five minutes night and morning. This consisted of holding a light wooden spatula between the lips and while doing so they did active movements, either exercises or playing a game. By doing so they developed the power of breathing deeply through the nose and at the same time holding their lips tightly closed unconsciously, because if they were going to hold a stick in their lips they were not thinking in terms of closing the mouth, but merely of holding the stick, and thus they developed the habit of breathing deeply with unconscious closing of the lips.

Dr. L. Stein said that the approach which Mr. Gwynne-Evans had outlined was a method of approach which he had used for many years in speech therapy. In any case of disturbance it was always the lower level that took over and became dominant. Thus, it was not a loss of function which was encountered but rather a different pattern of function according to what was dominant on that level. Miss Van Thal had referred to the use of such games as pretending to be a fish and so forth. The appeal was to the child's primeval instinct, and by this means the muscle tone was increased, because that was closely associated with the emotional meaning. He did not think that tone could be increased by mere exercises but it could be increased if it was correlated with an emotional attitude.

F. C. W. Capps, in reply to Mr. Musgrave Woodman, said that the splints stayed in all night. In the use of hundreds of splints it had never been necessary to retrieve one from the œsophagus. They had to be taken out during meals.

A. A. Nove, in reply to questions, said that one of two reflexes occurs in the presence of a foreign body in the mouth: one, to eject it, the other to swallow it. During consciousness the desire would be to retain it because of the sense of comfort experienced by the different structural units being correlated correctly. In sleep there was occasionally a tendency during the early stages of wearing the appliance for it to be ejected, but whilst the appliance remained in the mouth, the act of swallowing, which normally took place, caused it to be engaged by the lingual surfaces of the upper and lower teeth as well as by the palate. As its external surface was a negative of the lingual surfaces of the teeth, palate, and mandible it brought about intermittent intermaxillary immobilization. Therefore, while the Andresen splint was easy to eject, it was impossible to swallow. With regard to prominent teeth, reconstruction included the alignment of the teeth. With regard to thumb sucking, in his view it was an indication that the child needed space in the mouth as well as support for the musculature and supplied that need instinctively.

Joan Van Thal said that she had not been able to give a full description of all the exercises, but these did include holding some object between the lips, such as a quill, which was a playful substitute for the pipe. The under-sixes learned to blow the nose, also to play the games which encouraged them to keep their mouths shut; it was the actual breathing exercises for thoracic expansion which were omitted in their case.

ILLUSTRATIVE CASE [*Abridged report*]

R. W., aged 4 years.

History.—Mouth-breathing day and night; snoring and disturbed sleep; recurrent colds; few sore throats. Adenoids removed elsewhere two years ago.

Upper respiratory musculature.—1.6.44: Orbicularis oris and muscles of facial expression relaxed; mandible released; no speech defects other than slight insufficient nasal intonation; inadequate palatal depression, with failure to elevate and retract posterior mass of tongue in closure of the faucial isthmus; tip of tongue abuts against pre-maxilla. Profile radiographs: adenoid shadow insignificant; shadow of palatal velum midway between post-nasal and oral air spaces.

patient was either admitted to the ward for two weeks, and three times daily inhaled a 5% carbon dioxide - 95% oxygen mixture through a B.L.B. mask for about fifteen minutes, or the child attended as an out-patient once a week and had inhalational therapy prior to breathing exercises.

Observation under the fluorescent screen of the response in the case of G. C. furnished interesting data: Told to take a deep breath the boy moved his shoulders up and down, and diaphragmatic descent was almost nil. While inhaling the mixture of carbon dioxide and oxygen, clavicular breathing was spontaneously replaced by costo-diaphragmatic action. Without the mask, performing his breathing exercises, the extent and rhythm of the costo-diaphragmatic excursion were maintained to the same degree. This observation demonstrates that breathing exercises can set up normal respiratory behaviour. Often it is more practical to do such exercises than to inhale carbon dioxide and oxygen in order to stimulate the reflex response.

Unless intelligent co-operation from the mother is assured, breathing exercises are not given to children below the age of 6.

Care is taken to eliminate the common error of raising the cage of the thorax under the illusion that this is tantamount to expanding it. Exercises and games are devised to encourage relaxation, flexibility and rhythm of the costo-diaphragmatic musculature rather than attempting to increase capacity.

Attention to posture is maintained throughout. The child may be referred to the physiotherapy department later.

Weekly attendance is advocated for a period of about three months and after that, fortnightly or monthly for another six months, with home practice between hospital attendances. Each child attending for respiratory rehabilitation has twenty minutes' individual attention. Children attending for ephedrine displacement are given a few minutes of routine exercises immediately after that treatment has been carried out.

Some of the playful exercises for the facial muscles and upper airway are carried out as follows:

(a) Observation of the difference between an open and a closed mouth: (1) By visual means; (2) by noting the different sensation when the lips are parted and when they are in contact. *For example*, the child pretends to be a fish, swimming about opening and shutting its mouth.

(b) Maintaining closure of the lips. *For example*, the patient sits in front of a mirror mainly occupied by listening to a story or something else that holds his interest, and at the same time is watched to see if his lips remain shut. This alternative occupation avoids stress.

(c) Intermittent clearance of the upper airway. Encouraging use of the upper airway.

(1) The child pretends to smell flowers or to be a dog sniffing at its dinner; (2) a game of blowing at some object such as a feather through the nose to hit a target; (3) using nasal resonance, i.e. humming.

The Chairman (Brigadier Myles Formby) said that the great importance of team work in a problem of this nature had been shown. It had been emphasized how wrong it was to anticipate that by dealing with one aspect only of a problem such as this, successful results would be obtained in anything but a very small percentage of cases. He had in mind particularly the removal of the tonsils and adenoids to remedy such conditions as mouth-breathing. Many must have felt bitter disappointment on finding that the child after operation went on as before, with his faulty breathing.

E. Musgrave Woodman, after thanking the openers for this broad and interesting survey of the problem, asked for further practical details about the interdental splint. How long was it worn during the day? Was it taken out for meals? On how many occasions had it to be retrieved from the œsophagus? It would be interesting to learn from their dental colleagues how they overcome the difficulty of the long central incisors which frequently projected over the lip and prevented the lips from coming together. One was accustomed to dental splints for restraining the line of the teeth. Did the interdental splint take the place of the metal retention apparatus wholly or in part?

C. P. Wilson said that the opener's demonstration had been a revelation, and if he made any criticism he hoped it would not be considered out of place. He was sorry that

no mention was made of the type of patient with what he might call the short upper lip. They had heard nothing at all about the importance of the use of the lips as a factor in moulding the shape of the jaws and mouth in addition to the splinting apparatus.

He understood Miss Van Thal to say that it was not practicable to do anything in the way of breathing exercises with children under 6. With this he disagreed. Miss Van Thal had also said that it was important that the child itself should observe if it was opening its lips during breathing exercises. His own feeling was that the most important thing was that the child should close its lips unconsciously, not consciously, and there was a simple way of making the child do that, namely by the holding of something in the lips. His own practice had been to make children do breathing exercises for five minutes night and morning. This consisted of holding a light wooden spatula between the lips and while doing so they did active movements, either exercises or playing a game. By doing so they developed the power of breathing deeply through the nose and at the same time holding their lips tightly closed unconsciously, because if they were going to hold a stick in their lips they were not thinking in terms of closing the mouth, but merely of holding the stick, and thus they developed the habit of breathing deeply with unconscious closing of the lips.

Dr. L. Stein said that the approach which Mr. Gwynne-Evans had outlined was a method of approach which he had used for many years in speech therapy. In any case of disturbance it was always the lower level that took over and became dominant. Thus, it was not a loss of function which was encountered but rather a different pattern of function according to what was dominant on that level. Miss Van Thal had referred to the use of such games as pretending to be a fish and so forth. The appeal was to the child's primeval instinct, and by this means the muscle tone was increased, because that was closely associated with the emotional meaning. He did not think that tone could be increased by mere exercises but it could be increased if it was correlated with an emotional attitude.

F. C. W. Capps, in reply to Mr. Musgrave Woodman, said that the splints stayed in all night. In the use of hundreds of splints it had never been necessary to retrieve one from the œsophagus. They had to be taken out during meals.

A. A. Nove, in reply to questions, said that one of two reflexes occurs in the presence of a foreign body in the mouth: one, to eject it, the other to swallow it. During consciousness the desire would be to retain it because of the sense of comfort experienced by the different structural units being correlated correctly. In sleep there was occasionally a tendency during the early stages of wearing the appliance for it to be ejected, but whilst the appliance remained in the mouth, the act of swallowing, which normally took place, caused it to be engaged by the lingual surfaces of the upper and lower teeth as well as by the palate. As its external surface was a negative of the lingual surfaces of the teeth, palate, and mandible it brought about intermittent intermaxillary immobilization. Therefore, while the Andresen splint was easy to eject, it was impossible to swallow. With regard to prominent teeth, reconstruction included the alignment of the teeth. With regard to thumb sucking, in his view it was an indication that the child needed space in the mouth as well as support for the musculature and supplied that need instinctively.

Joan Van Thal said that she had not been able to give a full description of all the exercises, but these did include holding some object between the lips, such as a quill, which was a playful substitute for the pipe. The under-sixes learned to blow the nose, also to play the games which encouraged them to keep their mouths shut; it was the actual breathing exercises for thoracic expansion which were omitted in their case.

ILLUSTRATIVE CASE [*Abridged report*]

R. W., aged 4 years.

History.—Mouth-breathing day and night; snoring and disturbed sleep; recurrent colds; few sore throats. Adenoids removed elsewhere two years ago.

Upper respiratory musculature.—1.6.44: Orbicularis oris and muscles of facial expression relaxed; mandible released; no speech defects other than slight insufficient nasal intonation; inadequate palatal depression, with failure to elevate and retract posterior mass of tongue in closure of the faucial isthmus: tip of tongue abuts against pre-maxilla. Profile radiographs: adenoid shadow insignificant: shadow of palatal velum midway between post-nasal and oral air spaces.

SERIAL RADIOGRAPHS OF PALATO-LINGUAL MUSCULATURE AT PHYSIOLOGICAL REST

1.6.44	Palato-lingual space wide open		
		Without appliance	With appliance
29.6.44	P.L.S.	Wide open	Wide open
13.7.44	P.L.S.	Open	Open
31.8.44	P.L.S.	Open	Just open
21.9.44	P.L.S.	Just open	Just open
26.10.44	P.L.S.	Just open	Closed
2.11.44	P.L.S.	Closed	Closed
Tonsils persistently inflamed— removed			
30.11.44	P.L.S.	Just open	Closed
25.1.45	P.L.S.	Just open	Closed
25.6.45	P.L.S.	Closed	Closed

Present state.—25.6.45: *Posterior oral musculature*: adequate palatal depression, with elevation and retraction of tongue in reflex closure of faucial isthmus.

Anterior oral musculature: orbicularis oris and muscles of facial expression have partly regained their tone; mouth remains closed most of the day. There is a tendency for the mouth to drop open at night. Sleeps quietly with appliance in oral cavity.

Comments.—Mouth-breathing controlled by posterior musculature; habitual closure of orbicularis oris not completely obtained.

Section of Anæsthetics

President—FRANKIS T. EVANS, M.B., D.A.

[May 4, 1945]

Anæsthesia in Operations for Closure of Patent Ductus Arteriosus [Abridged]

By JOHN GILLIES, M.B., F.R.C.S.Ed., D.A.

THE ductus arteriosus is a foetal vascular structure which during intra-uterine life forms a wide channel of communication between the pulmonary artery and the distal part of the arch of the aorta. It conveys venous blood from the right side of the heart to the aorta thus by-passing the non-functioning lungs. At birth, when the lungs expand, the right and left pulmonary arteries assume their full function and the ductus arteriosus like the foramen ovale closes. Such closure which is functional at first is facilitated by the spiral arrangement of the muscle in the ductal wall (von Hayek, 1935) producing a torsional effect as the muscle contracts. Subsequent anatomical obliteration by subendothelial cicatrization, whereby the ductus is changed to the non-patent ligamentum arteriosus, is more gradual but closure is usually complete by the end of the first post-natal month. If for any reason the ductus remains open, then a shunt or arteriovenous fistula is established between the aorta and the pulmonary artery. Because of the higher pressure in the aorta as compared with the pulmonary artery blood flows from the former to the latter. Thus, as much as 50% or more of the left ventricular output may be directed through a patent ductus on a futile journey through the lungs. Several effects follow:

- (1) Intrapulmonary pressure is increased, the branches of the pulmonary artery dilate and the lungs become more vascular than normal. Slides of telerradiograms illustrate these features, the enlarged pulmonary artery showing as a bulge between the arch of the aorta and the ventricular mass. Telerradiograms taken after operation show marked modification and a return to normality in the heart and lung shadows.
- (2) Right ventricle hypertrophies in response to increased pulmonary pressure.
- (3) Volume of blood getting past ductal opening into descending aorta during each ventricular contraction is small and there is a characteristic low diastolic pressure. Slides of anæsthetic charts show that the pre-operative low diastolic pressure and high pulse pressure are transformed to normal by successful obliteration of the shunt. The marked rise of diastolic pressure sometimes appeared to be initiated by the actual handling of the ductus during its dissection and the placing of the ligatures. In other cases there was no change until the abrupt rise in pressure which immediately followed the occlusion by ligation.

It may be mentioned that oxygenation in the patient with a simple patent ductus is usually adequate and cyanosis is not a feature unless some other congenital defect such as pulmonary stenosis is co-existent. Violent exercise or prolonged crying

may create a rise in pulmonary pressure sufficient to cause a temporary reversal of flow in the ductus and cyanosis in consequence (Abbott). During anaesthesia the high pulse pressure may rise and the diastolic pressure fall owing to vasodilation and an increase in cross-section area of the peripheral vascular bed.

Two categories of patients may be presented for operation. First, young children, 4 to 12 years or so with simple, uninfected patent ductus, showing lack of physical development and early signs of congestive heart failure. Operation to terminate the abnormality and prevent if possible the more serious complication of bacterial endarteritis is considered justifiable. Secondly, young subjects in their teens who have led a fairly normal life until infection has occurred. Toxaemia, septic emboli in the lungs, and some degree of congestive heart failure make this latter group very poor risks from the anaesthetic point of view but surgical treatment is the only hope for such patients and the successful results reported by Tubbs, Touroff, and others justify the risk.

It is important that the anaesthetist should appreciate the surgeon's problems. Slides of the anatomy of the operation field show the relations of the great vessels, the left phrenic and left recurrent laryngeal nerves, and the left bronchus, to a patent ductus. They indicate also the difficulties of the surgical procedure especially those due to a very short, wide ductus and to adhesions. Nerve trauma resulting in diaphragmatic and vocal cord paralysis may occur but the most serious danger is haemorrhage during the separation and isolation of the ductus particularly from behind and below where it may be adherent to the bronchus. If the ductus is infected and friable this danger is much greater. For this reason a slow intravenous blood drip is advisable in order that replacement can be made immediately should serious haemorrhage occur. The anaesthetist must maintain a close watch on such a drip not only to ensure that it is ready against any emergency but also in order to see that in the uneventful case the patient does not get too much, because it must be remembered that when the ductus is occluded the volume of blood passing into the aortic distribution will be much augmented almost as if the patient had given himself a transfusion.

The series of cases with which I have been associated dates from October 1940 and I should like here to acknowledge the debt I owe to the physician and surgeons concerned, Dr. Rae Gilchrist, Sir John Fraser, Bt., and Mr. Walter Mercer, for permission to use their records in the preparation of this paper. The experience was a limited one embracing 21 ligations, the operation being performed twice on one patient. In only three cases was infection present. Anaesthesia for the uninfected and younger subjects presented little difficulty. It is familiar knowledge that children tolerate thoracotomy much better than older subjects and exhibit a remarkable resiliency in recovery so much so that Gross gets his young patients up in 24 hours and ambulatory in three days. The more ill patients, viz. those with infection present, were in a somewhat critical condition during operation. Their physical state which is bad to begin with may deteriorate rapidly during the operation. Adequate oxygenation may be difficult because of patchy areas of consolidation in the lungs as a result of emboli coming from the infected vessels.

Although the management of the anaesthesia for this operation is not essentially difficult it must be of such a quality that the surgeon gets maximum assistance in his delicate manipulations. Thus the quietest respiration consistent with good oxygenation must be maintained. A high oxygen content helps oxygenation by continuous diffusion into the alveoli when respiratory excursion is reduced. Quiet breathing will also minimize mediastinal movement. If necessary, controlled or assisted respiration may be employed if anoxaemia threatens. It is advantageous to make use of as much of the lung on the open side as possible so long as the surgical procedure is not hampered. Cyclopropane has been employed almost entirely in this series with satisfactory results. In the cases performed by Gross of Boston and Jones of Los Angeles cyclopropane has also been the agent preferred. The use of a tracheal tube is not essential but is a comforting safeguard against mechanical obstruction of the airway.

Cardiac arrhythmia is sometimes seen. This may arise as a result of excessive or prolonged retractor pressure on the mediastinum and can be corrected by stoppage of the operation for several minutes. Deep cyclopropane anaesthesia may also cause arrhythmia particularly if the anaesthetist fails to prevent anoxaemia by assisting the patient's respiration in good time.

Complete deflation especially under prolonged pack or retractor pressure sometimes makes for difficulty in re-expanding the lung. Jones interrupts the operation in order that the anaesthetist may re-inflate the lung for a few seconds every ten minutes. This is a definite aid in facilitating the final re-expansion at the end of the operation and of mitigating post-operative pulmonary complications.

The technique of re-expanding the lung at the conclusion of the operation merits careful attention. The use of positive pressure through a tracheal tube is not entirely satisfactory. Apart from the possibility of driving mucus downwards into the ultimate bronchioles with the risk of blocking them there may also be produced trauma by the injudicious use of pressure and a disturbance of circulatory dynamics from mediastinal movement during the manœuvre. The induction of negative pressure in the pleural cavity after closure of the chest wall is preferable. This may be done by means of a stiff catheter passed through the wound and secured by a purse-string suture which provides good closure when the catheter is withdrawn. Air may be exhausted by means of a pneumothorax apparatus.

The pathological and surgical aspects of patent ductus arteriosus may appear to have received predominant attention in this paper but one feels that a very adequate knowledge of those factors must accompany even the highest degree of technical skill on the part of the anæsthetist if the high standard of success which is possible in the surgical treatment of this condition is to be achieved.

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Mr. O. S. Tubbs said that he had operated upon 14 cases of patent ductus arteriosus, 11 of which were complicated by infection. Cyclopropane had been used in the first 13, but the most recent case had been anæsthetized with ether and oxygen given through a closed circuit. The change of agent had been made because extreme tachycardia (> 200) had occurred in two patients when using cyclopropane; the tachycardia was clearly due to the anæsthetic as it appeared before the operation had proceeded further than the skin incision. The case in which ether was employed was exceedingly ill due to superimposed infection (no radial pulse or registrable blood-pressure was present) and yet withstood the operation remarkably well. In view of this experience and similar satisfactory results using ether for pericardiectomy, the speaker favoured ether for cardiac surgery including ligation of the patent ductus.

He was surprised that no rise in diastolic pressure had been noted at the time of ligation of the ductus in the opener's series as it had almost invariably been obvious in his own cases. The opener's recommendation of an "intravenous drip" so as to be prepared for severe accidental hæmorrhage was endorsed, provided it was realized that these patients almost certainly had an increased blood volume so that the amount of intravenous fluid should be kept to an absolute minimum if no such hæmorrhage occurred.

Preparation of the Diabetic Patient for Operation

By GEORGE GRAHAM, M.D.

BEFORE the introduction of insulin in 1923 very few operations were performed on diabetic patients. Nowadays diabetes is in no wise a contra-indication for any operation provided that (1) a physician is at hand who knows how to look after these patients; (2) adequate facilities are available for estimation of the blood sugar, &c.; (3) the best anæsthetic is chosen and given by a good anæsthetist; and (4) that the operation is well and quickly done.

That is, if all the conditions are ideal, the risk of operation is very little more than in the case of the non-diabetic of equal age. It is important to make certain that the diagnosis is correct. The presence of glycosuria does not necessarily prove that the patient has diabetes since he may have a low threshold to the kidney and a normal sugar tolerance.

The anæsthetic is very important and a local or spinal anæsthetic causes least disturbance. Gas and oxygen is the next best provided sufficient oxygen is given to prevent any cyanosis since the blood sugar is always raised by cyanosis. The intravenous anæsthetics, pentothal and evipan, come next and I have seen no ill-effect from these. Ether which may be necessary to get complete relaxation with gas and oxygen does raise

the blood sugar and should be used only in small amounts. Avertin is better not used because it is said to lower the glycogen in the liver by 50%, and so renders the liver more liable to damage. Finally, chloroform should never be used because of its action on the liver.

When an operation has to be performed the diabetic condition should be as well controlled as possible. If the diabetic condition is mild and the patient is not taking any insulin but having a small amount of carbohydrate, say 100 grammes or less, he runs some danger of liver damage because of the low glycogen content. It is better in these cases to increase the carbohydrate to at least 150 grammes and to give a small dose of insulin, 1 unit for every 4 to 5 grammes of extra carbohydrate. For an extra 50 grammes I would give 10 units; 6 units in the morning and 4 units at night for two to three days before operation. The patient will probably be able to give up insulin a few days after the operation, provided there are no complications. If the patient is having insulin but is passing a good deal of sugar and the operation is not being done in an emergency, it is better to increase the insulin for a few days and thus stabilize the condition. If, however, the patient belongs to the class which is liable to have overdoses when any attempt is made to get the urine sugar free, it is better not to make any change. The type of insulin must also be considered. I think it is much better to use the ordinary or quick-acting insulin in the preparation of the patient instead of the slow-acting insulins, since these do not act quickly enough to control the rise in the blood sugar caused by the anæsthetic and are more likely to cause hypoglycemia. It is better to allow two to three days for the change-over. If the patient is taking one dose of protamine zinc or globin insulin, say 20 units, he should be given 12 units in the morning and 8 units at night of the ordinary insulin. This may fail to control the glycosuria or may cause attacks of hypoglycemia, but in two or three days the correct dose should be easily determined. If bigger doses are being taken they should be split in the same manner. Thus with 50 units of protamine zinc or globin insulin 30 + 20 should be given. If he is taking a mixture of ordinary and protamine zinc or globin insulin, say 12 units of ordinary and 8 units of protamine zinc or globin, the morning dose should be 12 units of ordinary and the evening dose 8 units of ordinary, but the evening dose may have to be increased by 2 or 4 units.

On the day of operation.—Morphia is always given to quieten the patient, but it tends to make the patient's breathing more shallow and increases the tendency to anoxia; the dose should be as small as possible, say 1/6th grain of morphia.

It is most important that the patient should not be starved before operation as this will reduce the amount of glycogen in the liver. He should have his usual feeds at bedtime and in the morning he should have at least 50 grammes of glucose in order to ensure that there is plenty of glycogen in the liver and muscles. He can of course have more than this if he is in the habit of taking it at breakfast. The dose of insulin must be varied according to the type of anæsthesia used, since it depends on two factors: (1) The amount of carbohydrate usually taken at breakfast; (2) the type of anæsthetic used.

(1) If he takes 50, 60 or 70 grammes of carbohydrate at breakfast he should be given 50, 60, or 70 grammes of glucose and his usual dose of insulin together with a supplement depending on the type of anæsthetic. If, however, he takes less than 50 grammes of carbohydrate, say 25 grammes, he should be given 50 grammes of glucose with a supplement for the extra 25 grammes and a supplement for the anæsthetic. The supplement for the carbohydrate is calculated on the basis of 1 unit of insulin taking care of 4 or 5 grammes of carbohydrate. Thus for the extra 25 grammes of carbohydrate the patient should be given an extra 6 units over and above his usual dose.

(2) The type of anæsthetic. If a local or spinal anæsthetic or gas and oxygen is being used I do not think that there is any need to give a supplement, but if gas and oxygen are being used with ether I think that at least 10 units should be given. In the case of pentothal I think that the supplement should be small, say 2 or 4 units in addition to the usual dose. The insulin should be given half an hour before the sugar which is best flavoured with lemon or orange juice. It is better not to put it into tea as this large dose of sugar spoils the taste of the tea.

The sugar should be given two hours before the time for the operation. There are no difficulties when the operation is to take place round 9, but it is more difficult when the operation is after this time. If the operation is timed for 12 noon to 3.30 p.m., say, he should be given his usual breakfast and insulin at the ordinary time. Then two hours before the time of the operation he should have 10 units of insulin followed by 50 grammes of glucose in place of the usual midday meal. If the operation does not

take place till after tea the usual midday meal should be taken without any extra insulin, the extra sugar and insulin being taken as usual two hours before the operation. Finally, if the operation takes place after the evening meal the arrangement should be made on the same principles as for the morning meal.

If the dose of insulin and sugar is arranged somewhat on these lines the anæsthetic will not do the diabetic condition any harm. The only complication which may occur is hypoglycæmia. This will not show itself during the operation as this, together with the anæsthetic, will certainly cause a rise in the blood sugar. The mild symptoms will probably pass unnoticed but the patient may not recover consciousness at the right time after the operation in which case an intravenous injection of glucose should be given.

TABLE I.

Usual breakfast carbohydrate Grammes	Usual insulin Units	Dose of glucose Grammes	Dose of insulin Units	Extra insulin for anæsthetic		
				Local	Pentothal	Ether
25	30	50	36	0	2 or 4	10
50	30	50	30	0	2 or 4	10
60	30	60	30	0	2 or 4	10

I have seen this occur once only. The patient had been given pentothal with gas and oxygen for a perurethral resection of a prostate gland. He had not regained consciousness some three hours after the operation; he seemed asleep but otherwise normal. I estimated the blood sugar at once and found that it was 50 mg.%. I injected 10 c.c. of a 25% solution of glucose about forty-five minutes after the blood was collected and he woke up immediately.

Preparation for an emergency operation.—If the patient has been taking insulin and is not passing sugar the size of the dose of insulin and glucose is decided as for the set operation. If, however, the patient is passing a good deal of sugar and some acetone bodies, the supplementary dose of insulin for the anæsthetic should be increased. If a local or spinal anæsthetic is given a supplement of at least 10 units should be given; if pentothal is used the supplement should be 14 or 16 units and if ether is given it should be 20 to 25 units. Though this may be sufficient for the anæsthetic, the patient may need much more after the operation. If he is very ill, and passing much sugar and much acetone bodies and operation is urgent, much bigger doses both of insulin and sugar should be given. The dose of sugar should be increased to 100 grammes to make quite certain that there is plenty of sugar in the body and 100 units of insulin should be given. It is in this type of case that estimations of the blood sugar are most valuable both before and after operation. Big doses of insulin will be needed after the operation if coma is to be prevented, and the blood sugar should be estimated at frequent intervals.

A Brief Account of Anæsthetics given in a Field Surgical Unit in the B.L.A.

From June 7 to November 10, 1944.

Major Rex Binning landed with his unit and one three-ton truck on the morning of D plus one and worked with the 30th Corps. After a period of static warfare in the bridgehead his unit went south of the Falaise gap to Argentan and thence crossed the Seine to Amiens and Brussels and the period under review ended at Nijmegen. During this time the unit set up the operating theatre on 12 occasions and a total of 584 cases were operated on.

The facilities for resuscitation were even better than in previous campaigns. There were more Field Transfusion Units than ever before. The superiority of blood over plasma in the resuscitation of battle casualties was again demonstrated. The result of the excellent transfusion service was that more very bad-risk cases survived long enough to be considered for operation. Given unlimited transfusion facilities it is almost impossible to say that any case is hopeless. Almost all our severe casualties were therefore given a chance.

the blood sugar and should be used only in small amounts. Avertin is better not used because it is said to lower the glycogen in the liver by 50%, and so renders the liver more liable to damage. Finally, chloroform should never be used because of its action on the liver.

When an operation has to be performed the diabetic condition should be as well controlled as possible. If the diabetic condition is mild and the patient is not taking any insulin but having a small amount of carbohydrate, say 100 grammes or less, he runs some danger of liver damage because of the low glycogen content. It is better in these cases to increase the carbohydrate to at least 150 grammes and to give a small dose of insulin, 1 unit for every 4 to 5 grammes of extra carbohydrate. For an extra 50 grammes I would give 10 units; 6 units in the morning and 4 units at night for two to three days before operation. The patient will probably be able to give up insulin a few days after the operation, provided there are no complications. If the patient is having insulin but is passing a good deal of sugar and the operation is not being done in an emergency, it is better to increase the insulin for a few days and thus stabilize the condition. If, however, the patient belongs to the class which is liable to have overdoses when any attempt is made to get the urine sugar free, it is better not to make any change. The type of insulin must also be considered. I think it is much better to use the ordinary or quick-acting insulin in the preparation of the patient instead of the slow-acting insulins, since these do not act quickly enough to control the rise in the blood sugar caused by the anæsthetic and are more likely to cause hypoglycemia. It is better to allow two to three days for the change-over. If the patient is taking one dose of protamine zinc or globin insulin, say 20 units, he should be given 12 units in the morning and 8 units at night of the ordinary insulin. This may fail to control the glycosuria or may cause attacks of hypoglycemia, but in two or three days the correct dose should be easily determined. If bigger doses are being taken they should be split in the same manner. Thus with 50 units of protamine zinc or globin insulin 30 + 20 should be given. If he is taking a mixture of ordinary and protamine zinc or globin insulin, say 12 units of ordinary and 8 units of protamine zinc or globin, the morning dose should be 12 units of ordinary and the evening dose 8 units of ordinary, but the evening dose may have to be increased by 2 or 4 units.

On the day of operation.—Morphia is always given to quieten the patient, but it tends to make the patient's breathing more shallow and increases the tendency to anoxia; the dose should be as small as possible, say 1/6th grain of morphia.

It is most important that the patient should not be starved before operation as this will reduce the amount of glycogen in the liver. He should have his usual feeds at bedtime and in the morning he should have at least 50 grammes of glucose in order to ensure that there is plenty of glycogen in the liver and muscles. He can of course have more than this if he is in the habit of taking it at breakfast. The dose of insulin must be varied according to the type of anæsthesia used, since it depends on two factors: (1) The amount of carbohydrate usually taken at breakfast; (2) the type of anæsthetic used.

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Section of Radiology

President—J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

[March 16, 1945]

Radiology of the Small Intestine

By JOHN WILKIE, M.B., Ch.B., M.Sc., D.M.R.E.

It would be well to review the normal radiographic appearance of the small intestine before considering the pathological. Everyone is familiar with the feathery appearance seen in the upper loops of the jejunum due to its deep mucosal folds which decrease in size as the gut approaches its termination. The walls of the ileum frequently appear smooth although gentle compression will often demonstrate low mucosal folds. In infants the mucosal folds are fewer and much lower. This changes the radiographic features, for none of these folds can be shown under the age of 3 to 4 months, when they begin to give the feathery appearance seen in the adult. The bowel shows marked segmentation and the lumen is usually uneven, and may show discontinuity, the barium shadow appearing as separate and distinct boluses.

Methods of Investigation

Two methods are available: (1) *Abdominal radiographs*.—This is a most valuable contribution to the investigation of diseases of the small intestine.

(2) *Opaque media*.—Every radiologist knows the dangers of giving barium by mouth in cases of suspected obstruction and the colon should always be examined by means of an opaque enema to exclude any obstructive lesion there.

For investigation of the small intestine a mixture of about 2 oz. of BaSO_4 in watery suspension is recommended. The small quantity of barium enables a satisfactory examination of the stomach and duodenum to be made and the onset of emptying established. Radiographs are taken fifteen minutes after emptying has started and usually show satisfactory filling of the jejunum. Following this, radiographs are taken at half-hourly intervals up to two hours, after which the intervals may be extended. Throughout the investigation screen examinations are made.

This communication deals with only three groups of cases: (1) Three cases showing congenital abnormalities. (2) Some changes seen in deficiency diseases. (3) Some cases of Crohn's disease.

The first two cases under Group I show the radiological findings associated with embryological malrotation of the gut. This may give rise to obstruction in the lower duodenum and the outstanding clinical feature is persistent vomiting, usually occurring shortly after birth.

Of the total of 584 cases 92 were anaesthetized with pentothal followed by cyclopropane. These were mainly the penetrating wounds of the abdomen and the thoraco-abdominal wounds. The speaker had used this combination since the second battle of Alamein and was convinced that it was of the utmost value in these cases.

There were 91 casualties operated on under pentothal and nitrous oxide using the technique of intermittent injection described by Organe and Broad. These cases were the multiple wounds which took an hour or more to do and in which if pentothal alone had been used an excessive dose would have been required with the consequent prolonged period of unconsciousness. This was particularly undesirable during rush periods when the nursing staff were taxed to the limit. The speaker mentioned some of the many types of apparatus which had been evolved to apply this technique and demonstrated a simple method of securing the syringe to the arm-rest.

380 cases were operated on under pentothal alone.

5 cases were done under local analgesia. These were mostly brachial plexus blocks for compound fractures of the humerus in which the method was particularly indicated in that it enabled the patient to sit up while the travelling plaster was applied.

10 cases of burns had no anaesthetic except intravenous morphia.

The speaker concluded by paying tribute to the supply services which always kept up with the advance of the Army.

Section of Radiology

President—J. L. A. GROUT, M.C., F.R.C.S.Ed., F.F.R.

[March 16, 1945]

Radiology of the Small Intestine

By JOHN WILKIE, M.B., Ch.B., M.Sc., D.M.R.E.

It would be well to review the normal radiographic appearance of the small intestine before considering the pathological. Everyone is familiar with the feathery appearance seen in the upper loops of the jejunum due to its deep mucosal folds which decrease in size as the gut approaches its termination. The walls of the ileum frequently appear smooth although gentle compression will often demonstrate low mucosal folds. In infants the mucosal folds are fewer and much lower. This changes the radiographic features, for none of these folds can be shown under the age of 3 to 4 months, when they begin to give the feathery appearance seen in the adult. The bowel shows marked segmentation and the lumen is usually uneven, and may show discontinuity, the barium shadow appearing as separate and distinct boluses.

Methods of Investigation

Two methods are available: (1) *Abdominal radiographs*.—This is a most valuable contribution to the investigation of diseases of the small intestine.

(2) *Opaque media*.—Every radiologist knows the dangers of giving barium by mouth in cases of suspected obstruction and the colon should always be examined by means of an opaque enema to exclude any obstructive lesion there.

For investigation of the small intestine a mixture of about 2 oz. of BaSO_4 in watery suspension is recommended. The small quantity of barium enables a satisfactory examination of the stomach and duodenum to be made and the onset of emptying established. Radiographs are taken fifteen minutes after emptying has started and usually show satisfactory filling of the jejunum. Following this, radiographs are taken at half-hourly intervals up to two hours, after which the intervals may be extended. Throughout the investigation screen examinations are made.

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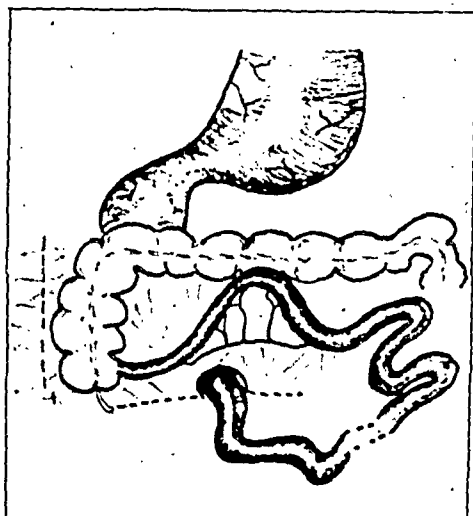
The first two cases under Group I show the radiological findings associated with embryological malrotation of the gut. This may give rise to obstruction in the lower duodenum and the outstanding clinical feature is persistent vomiting, usually occurring shortly after birth.

CASE I.—J. P., male aged 8 days. History of vomiting since birth. Not taking feeds. The vomitus was black and sometimes bile-stained.

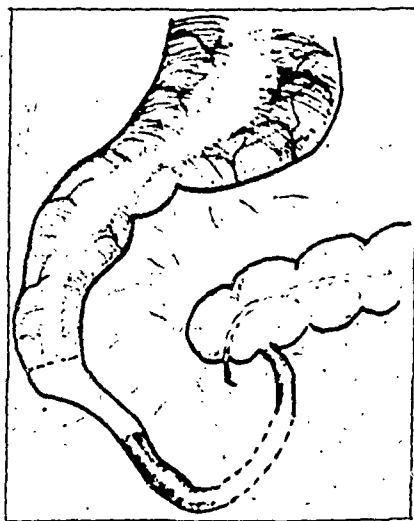
Barium meal examination showed a large gastric residue two and a half hours after the meal. There was gross dilatation of the duodenum down to the junction of the second and third parts. Such barium as had passed beyond was seen as a few scattered flakes.

A diagnosis of duodenal obstruction, probably associated with malrotation of the gut, was made.

At operation, the cæcum was found to be lying across the duodenum and to be bound down to the posterior abdominal wall by a membrane. Fig. 1 demonstrates the condition found and the operation undertaken. The patient survived only forty-eight hours.



(a)



(b)

FIG. 1.—Cæcum bound down across the duodenum. This was freed and replaced in its "primitive" position.

CASE II.—A. P., male aged 6 weeks. History of abdominal pain and copious vomiting of bile-stained material for four days. The infant was dehydrated and visible peristalsis was noted.

A barium enema showed the cæcum to be high and displaced towards the mid-line.

Barium meal examination showed a large gastric residue after three hours; within a few minutes of giving the meal, there was marked distension of the duodenum up to the junction of the second and third parts. Very little barium passed beyond this. Abdominal exploration revealed a common mesentery for the small intestine and colon. There was no pressure on the duodenum, but the mesentery was twisted, close to its origin (fig. 2). This had caused an obstruction at the duodeno-jejunal flexure. The "twist" was undone and the cæcum fixed in the right iliac fossa.

The clinical and radiographic features of both these cases are closely parallel. Radiography failed to distinguish between the two types of obstruction. Had it been possible in the second case to fill the duodenum up to the duodeno-jejunal flexure, where the obstruction was found, a more exact pre-operative diagnosis might have been possible.

The third case in this group is one of congenital atresia of the intestine. Again the presenting symptom was vomiting.

CASE III.—J. R., male aged 4 days. History of vomiting about three hours after every feed since birth. There was moderate dehydration, abdominal distension and some visible peristalsis.

Barium meal examination showed only moderate distension of the duodenum and upper coils of jejunum. This increased as the barium passed on, and violent to-and-fro movements were seen in the bowel. Even after twenty-one hours no barium had passed beyond the distended loop.

Exploration showed complete atresia low in the jejunum. A second obstructive diaphragm was found a short distance beyond the site demonstrated by the barium meal.

This emphasizes the importance of careful examination at operation, for there is no possibility of demonstrating the distal obstruction radiologically. Fig. 3 shows the condition found and the type of operation undertaken.

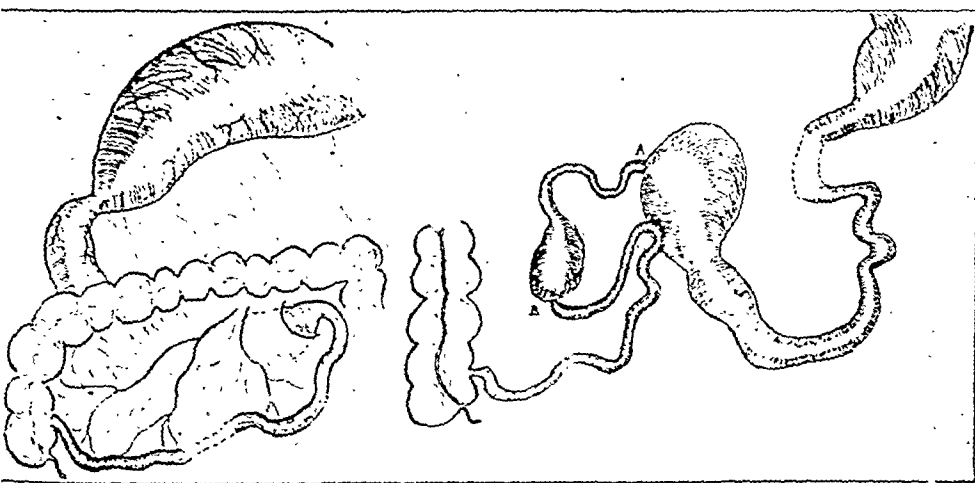


FIG. 2.

FIG. 2.—A. P. Diagram to show twisted mesentery and distension up to duodeno-jejunal flexure.

FIG. 3.

FIG. 3.—Obstruction found at A and B. That at B was shown by the secondary dilatation of the small bowel above it. Lateral anastomosis performed.

Radiological changes may also be demonstrated in the deficiency diseases. In the Carman Lecture for 1941, Ross Golden discusses these findings and groups the changes under three headings: (1) *Changes in motility*.—(a) Hypermotility, apparently in the earlier stages; (b) hypertonicity, usually in the earlier stages; (c) hypomotility, in the advanced stages; (d) dilatation, particularly of the jejunum in the advanced stages; (e) abnormal segmentation. Areas of spasm between which the lumen may be normal or of larger calibre.

(2) *Changes in the mucous membrane*.—(a) Coarsening of the folds; (b) obliteration of the folds.

(3) *Flocculation of the barium*.—Giving a coarsely granular appearance.

Golden also states that gas may be found in the small intestine in considerable amounts, and that fluid levels may be demonstrable.

With such variable findings, great caution must be exercised in the interpretation of results: a warning given by Golden.

The Author then showed three cases demonstrating some of the radiological changes described by Golden, and then continued: One of these three cases, fig. 4, shows the thickened mucosal folds, and in this case there was also considerable hypermotility, the small intestine being almost completely empty after two and a half hours.

The third group of cases shows the radiological features of Crohn's disease, and is included because of some superficial resemblances to the changes found in deficiency states. Clinical diagnosis of Crohn's disease in its chronic form depends upon the demonstration of a tender mass in the lower abdomen, diarrhoea, often with blood in the stools and intermittent pyrexia.

Radiological examination reveals some ileal stasis with varying degrees of localized dilatation and narrowing of the intestine. This narrowing is often so striking that the term "string sign" has been given to it. Although at one time considered diagnostic, it is now known that Crohn's disease may exist without giving this sign.

Three cases giving typical histories and characteristic radiological findings were shown. One of these, fig. 5, shows multiple areas of spasm and dilatation of the small

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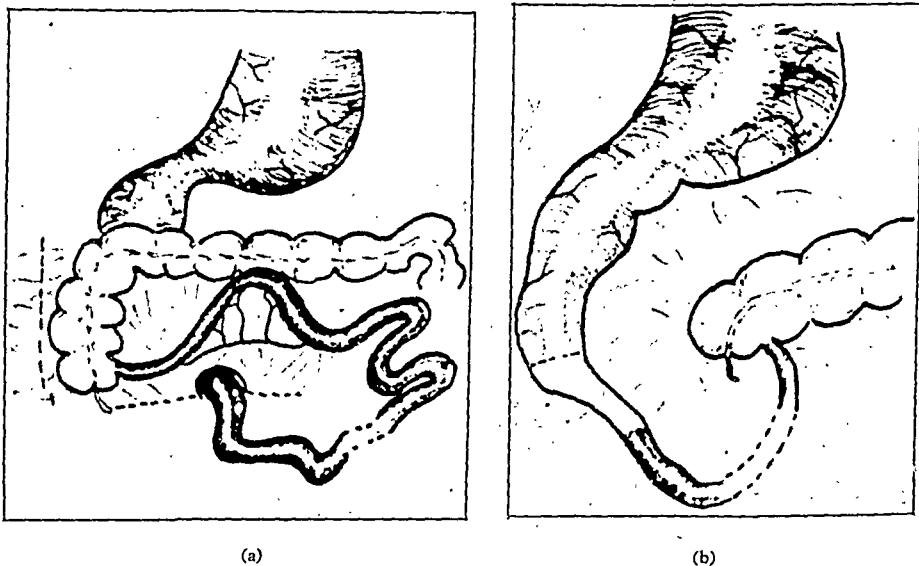


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Supporting Dr. Wilkie's advocacy of initial examination of colon and as much of small bowel as possible by barium enema, he asked if it were not usually simpler, in examining infants, to give the barium by the feeding bottle, thus ensuring that the correct quantity was ingested and eliminating the chance of deviations from normal mobility and appearance which might be due solely to fear, discomfort, &c.

Commenting upon the apparently large amount of barium which was evident in some of the films which Dr. Wilkie had demonstrated, he asked what was considered to be the optimum volume of contrast meal to administer by mouth to an adult, prior to detailed examination of the small bowel.

Dr. Wilkie, (in reply) suggested that four ounces of a watery suspension was a suitable quantity for most cases.

[May 18, 1945]

The Significance of the Latent Period which Elapses between Onset and Radiographic Appearances

By JAMES F. BRAILSFORD, M.D., Ph.D., F.R.C.P., F.I.C.S.

THOSE of us who have intimately followed the development in radiology throughout the past quarter of a century can remember the time when the radiographic demonstration of even the grossest lesions was not acceptable to the clinician: he preferred to be guided by his own clinical findings. By persisting in these demonstrations and proving by careful follow-up of the patients the accuracy of the radiological interpretation, radiologists have now so convinced the clinician of the value of the radiograph in diagnosis that the latter has performed a *volte-face*. Skill in eliciting and detecting early clinical signs and judgment of clinical evidence demand years of painstaking and time-consuming investigations: with to-day's rush and bustle these investigations are often lacking in thoroughness, consequently gross lesions are as frequently overlooked. Unfortunately it is the radiologist, who, usually unwittingly, provides the conclusive evidence of this neglect, consequently there is a desire not only to use radiology before clinical methods, but to use it without the aid or knowledge of the radiologist. The confidence to do this comes from the fact that at most meetings concerned with diagnosis, descriptions and discussions have centred around the radiographic appearances of well-established lesions, many clinicians and students are taught solely on positive radiographic evidence of the grossest nature. Most medical and surgical textbooks contain a very small selection of radiographs illustrating only advanced lesions. Such radiographs are provided by the radiologist at the request of the clinician for the teaching and examination of students. There is little or nothing said in the clinical lectures or written in the textbooks of the latent period, the early signs, the differential diagnosis or the sequence of radiographic appearances during development or as the result of treatment. Such knowledge can only be gleaned by those who devote themselves to the careful daily routine examination of hundreds of radiographs of patients about whom clinicians have helpfully indicated the essential clinical findings.

Because the radiographic signs are astonishing to the clinician in their grossness, at a time when the clinical signs are so trivial as to be overlooked, there is a tendency to neglect the clinical examination and use the short circuit of radiology. But a negative radiological report can be equally astonishing to a clinician who has seen very obvious clinical signs. Failure to appreciate the limitations and qualities of radiology, or to seek the helpful co-operation of the radiologist, results in unjust criticism of the radiologist, unreasonable condemnation of good quality radiographs and faulty interpretation of defective and good radiographs. The radiograph is but a measure of the relative densities of the structures traversed by the X-rays—visibility depends on the contrasted density of one structure in or against another of lesser or greater density.

A comparative macroscopic and radiographic study of such structures as the lungs or bones, the details of which appear to be so entire in the radiograph, readily reveals to the competent observer the fact that lesions have to attain a sufficient size or produce sufficient change before they will produce a contrast density which permits their detection on the

intestine. The differential diagnosis between tuberculosis ileitis and Crohn's disease is often extremely difficult or even impossible.

It has not been possible to consider every type of pathological condition, but an attempt has been made to draw attention to some of the less common lesions. No



FIG. 4.

FIG. 4.—Case of sprue. Shows thickened mucosal folds.



FIG. 5.

FIG. 5.—Case of Crohn's disease—unproved. Multiple areas of spasm and dilatation.

doubt opportunities for further radiological studies in deficiency states will be provided by large numbers of Service men returning from Prisoner of War Camps overseas.

Dr. A. S. Johnstone commented on two points arising out of the paper.

The first was the absence of gas in the colon—particularly the proximal portion—in cases of acute small bowel obstruction. This was due to vigorous peristalsis which passed on beyond the obstruction keeping both the distal segment of small bowel and the colon relatively empty and gas-free.

The second was Stierlin's sign, or spasm of the cæcum, which almost invariably accompanies regional ileitis when it involves a segment of lower ileum. The cæcum when outlined by barium resembles an inverted thumb.

Dr. C. G. Teall said it was important to realize that conditions other than steatorrhœa would give the abnormal bowel picture which had been described as being typical of that disease. He did not think it was possible to make a diagnosis of such conditions as sprue and steatorrhœa from the radiological appearances seen after a barium meal. In infants the radiological appearance of the small bowel normally showed the irregular filling and clumping and the absence of the "fleck" pattern which is associated with steatorrhœa. It was therefore impossible to recognize any change from the normal in coeliac disease at this age.

Dr. J. Blair Harley (Manchester) agreed that much positive information could be obtained from detailed study of the small intestine, but pointed out that the intestinal tract could also, on occasion, prove unexpectedly "silent". Illustrating this observation he described a recent case, a male aged 25, whose stomach and bowel, examined by him fourteen days after (proved) perforation of an acute jejunal ulcer, and only five to ten minutes prior to the occurrence of a second acute perforation (also proved), failed to reveal the slightest deviation from normal either in appearance, function, or "motility".

graphic control, but the necessity for radiographic control of treatment as had been indicated was not appreciated by the rehabilitation experts and disasters to joints occurred, which were now far worse for the patient than if no treatment had been sought and experienced.

There can be little more injurious advice than "Work and still more work" given by the rehabilitation officer who regards each injured person as a potential chronic invalid rather than what is usually the case, a person anxious to resume his normal activities. Even when the affected part is protected to some degree by a plaster case such advice can be very harmful. Perhaps only those who have experienced the inefficiency of immobilization of a plaster spica are able to realize that. A more careful study of Hilton's "Rest and Pain" is desirable.

I cannot help but consider that the surgeons are to blame for these disasters in so far as they deliberately failed to seek the helpful co-operation of their radiological colleagues. Obviously in any new work all the possible partners in the team will have only their specialist experiences to call upon: working isolated at the problem each would gain certain important knowledge in the other spheres, but this would be incomplete and misleading because of its lack of essential grounding. With reasonable co-operation of all members of the team, each contributing his specialized knowledge to a common pool and subjecting to common criticism, sound judgment would be reached at an earlier time with less danger and greater benefit to the patient and progress of the art.

No one to-day ought to wait for radiographic evidence of osteomyelitis before administering treatment, but it is done. As I have stated elsewhere radiographic evidence of acute osteomyelitis does not exist. It takes ten days or more from the onset of prominent clinical signs before the radiograph registers any change. Treated efficiently at the onset of clinical signs, complete resolution can be obtained--wait until radiographic signs and the bone may become the seat of chronic osteomyelitis, or the patient may lose his limb or even life. Radiographic signs of the infection may persist for many months even after effective treatment and clinical cure.

In malignant disease of any deep organ clinical signs and symptoms may be present for months to a year or so before there is radiographic evidence, but though there is a demand for earlier and yet earlier diagnosis, it is not always that the early radiographic evidence of malignant disease is accepted. One of the earliest carcinomas I have discovered in the stomach I found in a patient who was sent for examination because of a vague indigestion with some failing in health. The gravity of the three-monthly radiological reports over nine months was not accepted until a tumour could be felt and at laparotomy the carcinoma was found to be inoperable. Secondary metastases in bone may produce considerable pain for many months before the radiograph will be interpreted as showing confirmative evidence. Post-mortem examination of such cases will reveal far more extensive lesions than the radiographs indicated. But if there is one site in which carcinoma develops, which might be thought by the uninitiated to produce radiographic evidence, yet fails to do so, it is the rectum. Because of an experience with a close relative I will not conduct a barium enema examination on a patient requiring a second opinion, when the surgeon has detected a carcinoma of the rectum by digital examination. In the case referred to, the patient complained of a sensation of a mass in the rectum with pain and bleeding. Expecting that digital examinations had been made, for she had had two surgical operations to relieve her complaint, I carried out two barium enema examinations with an interval of several months, but, in spite of every care, I failed to detect any abnormality. It was only when I insisted that she be taken to a surgeon for the specific purpose of a digital examination that an inoperable carcinoma was discovered just within the anus.

I need hardly mention that there is a definite latent period between the appearance of clinical signs and radiographic signs in pregnancy. Except with the unfortunate demonstration of early fetuses on the uterine wall by the injection of lipiodol, no definite radiographic evidence can be detected within nine weeks of inception, but as I have indicated, even the full term foetus may not be recognizable on radiographs in some cases of osteogenesis imperfecta.

While there are some conditions in which the clinical signs are soon followed by radiographic evidence, there are others such as cysticercosis in which the clinical signs in some cases occur only during the initial infestation and then disappear, leaving the discovery of the infestation to a chance radiographic discovery five to ten years after, when the parasites have calcified. Prior to my paper on "The X-Ray

radiograph—large lesions can be produced yet the radiograph will not reveal them. It should not therefore be astonishing to realize that it takes time before radiographic signs become recognizable after the onset of any assault, whether it be on the patient or on the pathological process by medicaments, &c. The latent period in association with infectious diseases, i.e. that period which elapses between infection and the appearances of clinical signs, is well recognized, but it is not appreciated as much as it should be, that the clinical signs in the early stages of disease or following injury may be very prominent, yet the radiograph will still reveal no abnormality at the site, and, perhaps, even less is it recognized, that after the initial clinical signs have faded, the radiographic evidence may still be absent or so insignificant that it may be missed by any but the experienced observer, and that when the radiographic evidence is well marked the clinical signs may be insignificant. In other words the radiographic signs lag behind the clinical, both at the onset, throughout the duration and during resolution. The duration of the lag shows considerable variation in different conditions. While we must therefore think of a latent radiographic period between onset and signs, we must also think of that positive radiographic period which exists between the disappearance of clinical signs and the disappearance of radiographic signs. In some conditions radiographic evidence persists throughout the remainder of an apparently healthy life.

Failure to appreciate this discrepancy between clinical and radiographic signs has often had an unfortunate bearing on the treatment of the patient. In such an acute condition as lobar pneumonia some radiographic signs may appear within a few hours of the development of the acute clinical signs, and evidence of improvement in the radiographic appearances follows within a day or so of the crisis, but the lag has no influence on the treatment of the disease which is following its normal course.

But there are conditions which necessitate a knowledge of the sequence of the changes and an ability to estimate the age and phase of the lesions if successful treatment is to be applied.

Following trauma to a bone or dislocation of a joint the radiographic signs of damage may not be detected for weeks, months or even a year or so, during which time the initial signs and symptoms may have gone and the unfortunate patient may be encouraged or even compelled to use and destroy the limb or joint. To give but three instances of types of lesions in which this has occurred:—

Following trauma, to say the outer aspect of the thigh, the patient may complain of some pain or tenderness to pressure but the radiograph may show no departure from the normal for two to four weeks and then an ill-defined calcium deposit may become apparent in the soft tissues which is then usually associated with a tender deep-seated tumour and restriction of movement. As the trauma was often received during excitement, as in games or passion, it was overlooked by the patient and the progressive development of the lesion over a few weeks in a previously healthy person has led to the diagnosis of sarcoma and amputation of the limb. Following reduction of a dislocated joint, more commonly the hip-joint, the radiographs for some months have been interpreted as showing no abnormality. Because of the serious trauma the patient may be rested for a week or so, and then as the radiographic appearances are regarded as normal, the patient is permitted to get up, and is later encouraged to exercise the limb. The patient may complain of pain or discomfort, but, with the normal radiographic appearances, is told that, though as the result of the injury some pain must be expected, it is essential to use the limb; in some cases the threat has been given that a stiff limb would result if it was not exercised. As long as the patient retains his confidence in his surgical adviser he continues to use the limb in spite of pain, but ultimately, perhaps after a year or more, the progressive disability causes him to seek further advice, and then the radiograph may reveal ossification of capsular or ligamentous insertions, destruction of the articular surface or complete disintegration of the joint.

But the most common post-traumatic destruction has arisen from a failure to appreciate the latent period which elapses from the time of a fracture of such a structure as the femoral neck, to the appearance of radiographic signs of avascular necrosis of the head fragment. Pinning of the femoral neck was done and because the radiographs indicated good anatomical position the patient was allowed and encouraged to use the limb within a few weeks. The possibility of the bone developing plasticity, which would permit the pin to cut through the femoral head and neck, or the walls of the acetabulum, was not recognized. It had been indicated by serial radiographic examinations that this change did take place and lasted over a period of two to four years. The operative proceedings were all done, often without any consultation with the radiologist, under so-called radio-

graphic control, but the necessity for radiographic control of treatment as had been indicated was not appreciated by the rehabilitation experts and disasters to joints occurred, which were now far worse for the patient than if no treatment had been sought and experienced.

There can be little more injurious advice than "Work and still more work" given by the rehabilitation officer who regards each injured person as a potential chronic invalid rather than what is usually the case, a person anxious to resume his normal activities. Even when the affected part is protected to some degree by a plaster case such advice can be very harmful. Perhaps only those who have experienced the inefficiency of immobilization of a plaster spica are able to realize that. A more careful study of Hilton's "Rest and Pain" is desirable.

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"Diagnosis of Animal Parasites" to a meeting of this Section in 1924, when I demonstrated the radiographic appearances of calcified cysticerci, few cases of cysticercosis had been reported; but since then there have been many, but, unfortunately, those clinicians who have become interested, notably MacArthur and his assistants, have been obsessed by the positive radiographic evidence of the calcified parasites and have devoted their attention to this irrevocable condition, rather than to research for the acquirement of knowledge whereby the clinical signs of infestation may be recognized when there are no radiographic signs. With prompt treatment designed to kill the parasite when it is vulnerable, and before it has produced permanent harm, some good would result, whereas undetected they may produce symptoms continuously, even after calcification permits of visualization, yet little or nothing can be done about it, except talk. Though as a general rule the clinical signs precede the radiographic, we must recognize an important exception which proves the rule.

Metastases in the lungs, and any other lesions which do not induce localized reaction, notably hydatid cysts, may be shown on a radiograph in the early weeks of implantation, yet there may be few or no clinical signs until secondary complications develop, or until almost the whole of the lung tissue has been obliterated. Because of this radiography of the chest is essential as a part of the first radiographic examination for a bone or brain tumour. I need here only mention that in the majority of cases of brain tumour the prominent clinical signs are without any radiographic signs unless we employ contrast media for visualization.

The recognition of secondary sarcomata in the lungs has an important bearing on treatment. As far as our present imperfect knowledge goes prompt amputation offers the only cure, yet how often is this followed within a month or so by the demonstration of secondary metastases in the lungs. As far as my experience goes it is rare to be able to demonstrate metastases within two to four weeks of dissemination. I base this on their demonstration following amputation or surgical intervention when I presume the dissemination took place; but I realize from the experience that metastases may not appear for one or more years, that these early cases may have been due to dissemination prior to the surgery; which of course occurs.

The latent period is of great importance in assessing the relation of trauma to the development of sarcoma. Geschickter and Copeland mention five and a half months between trauma and radiographic appearances of Ewing's tumour. Personally I do not think it is possible to say, for I do not know what relation the one has to the other. Of all the thousands of injuries to bones which I have seen during the two wars and the interval between, I have seen but two genuine cases of sarcoma arising at the site of injury and in both there was a latent interval of about ten years between them. I have made it a practice to consider a lesion of a simple inflammatory nature in the first instance if the trauma and the radiographic signs suggest that the former is associated with the latter. Generally speaking the radiographic signs in sarcoma indicate a lesion which was well developed at the time of the trauma or the latter was so long before that conclusive evidence of its influence cannot be obtained. Because of the possibility of claim on this score it is important to radiograph every bone injury as soon as possible.

In the condition of silicosis clinical signs and symptoms may be present years before the radiographic evidence is sufficiently well marked to be accepted for compensation. It would appear that the lesion must have developed to a size readily measurable in a radiograph, which means very considerable irrevocable damage to the lung and invalidism before the clinical signs are given the significance they deserve. More attention to the early clinical and radiographic signs and the transference of the patient from the possibility of further inhalation of silica would appear to be the desirable humane aim.

But it is in tuberculosis that we are confronted with the importance of the latent period between infection and the appearance of radiographic signs, for, as tuberculosis is an infectious disease, we seek its diagnosis and segregation as a measure of preventive medicine, apart altogether from the question of treatment.

Tuberculosis of bones and joints is frequently manifested clinically months, and in some cases years, before typical radiographic evidence can be obtained. The early radiographic signs can be missed and mistaken, for, as I have shown and described, the disease is manifested by many different changes in the bones and joints. Auerbach and Stemmerman recently reported (July 1944) that "not a single correct diagnosis was

made in 30 (25%) of cases with tuberculosis of the spine, though in half of these the roentgenographic studies had been made within two months of death and in several cases within two weeks". I would not like to think that so large a percentage of errors was a common finding.

The latent radiographic period in pulmonary tuberculosis is of particular significance not only because of the variation in the clinical types, but because the radiographic evidence of the disease can persist after the clinical signs have diminished or disappeared. The subsequent progressive diminution of the radiographic signs may be striking for a time, but eventually the lesion may appear to become stabilized. Unfortunately we can only infer from periodical radiographic examinations that the disease has been stabilized in the past. We cannot, because of a further latent radiographic period which elapses after reactivation, a not uncommon occurrence, say that it is at present inactive. We may see serial radiographs of a patient taken at regular intervals for five or more years which indicate healed lesions. Even at the next examination, requested before the routine radiographic survey because the patient has developed symptoms, we see no change in the radiographic appearances; but at a subsequent examination an explanation of the symptoms may be seen in extension of the radiographic signs.

The delay at the onset of the initial and subsequent attacks in the appearances of radiographic signs is responsible for the failure to recognize the disease when radiography is substituted for clinical methods. We know that a good proportion of the people of these islands are infected at some time or other with tuberculosis for we see the evidence at post-mortem and frequently by chance radiography. Some lesions in the lungs completely resolve leaving no radiographic evidence. This not only applies to small, so-called minimal lesions, even those associated with marked radiographic evidence can entirely disappear with conservative home treatment; this includes such lesions as are associated with the radiographic appearances of miliary tuberculosis consolidation, cavitation or pleural effusion. It is not uncommon for a patient to have a number of such attacks and yet the residual radiographic evidence remain insignificant, i.e. we cannot estimate the extent or history of the diseases from the residual radiographic signs. Attacks of pneumonia associated with pleural effusion may occur at irregular intervals. Between the attacks the clinical signs may be absent and the radiographic signs gradually cleared. Any one of these attacks may be associated with considerable extension of the disease, which may be fatal. Certainly the radiographic evidence during these intervals may be such that it would be interpreted as indicating healed lesions. We have this knowledge from the periodical examination of patients who have been referred for radiographs, but we know from radiological examination of patients suspected to have other lesions that the nature of the illness is not always suspected by the doctor; or the patient with fears of the disease, avoids seeking confirmatory evidence because of the stigma which is attached to it with all its influence on his or her social and business life. In some cases the disease runs a rapid course and a patient, who previously was in good health and physique, goes down with a severe and protracted respiratory disease which at the first radiographic examination is revealed as extensive destruction of the lungs, and no matter what treatment is adopted progressive failing and exit occurs.

Between the mild and the fulminating types are to be found all grades of severity, some continuously progressive, some showing the irregular bouts with free intervals, many remaining healed after the first attack. Whenever the disease is progressive there are clinical signs. I base this on the experience that the earliest radiographic signs which I have seen have been in patients who were either contacts with open cases of pulmonary tuberculosis and had some evidence of respiratory disease or had begun to show such signs of enfeebled health that the doctors requested an X-ray examination or the patients had some reason to fear that they had contracted disease: or they were patients, who, previously well, had recently developed respiratory symptoms or failing health. In some cases where the doctor has not been satisfied with the negative radiographic opinion he has repeated his request at a later interval and obtained confirmatory evidence. Unfortunately the negative radiographic evidence at onset of the primary or the reactivation is apt to be relied upon as conclusive evidence of freedom from the disease and no further request is made until the worsening of the patient's condition demands it, and then frequently the evidence of extensive disease is only too apparent. From the point of view of preventive medicine this is very unfortunate for such a patient can unknowingly infect others. I do not believe that a patient can have progressive pulmonary tuberculosis associated with cavitation and fibrosis without some signs and symptoms and so escape detection at a sound clinical examination. If it were true that such conditions could

escape a sound clinical examination then I should regard the teaching of clinical methods as a waste of time and advise physicians and students to devote their time to a better training in radiology. My radiographic and clinical experience teaches me that tuberculosis does show a latent radiographic period and later in some cases a symptomless positive radiographic picture, the significance of which depends entirely upon the clinical condition of the patient.

I would urge that the practitioner's interest in tuberculosis be stimulated and that he be taught the significance of the negative and positive radiographic findings and that ready facility for complete radiological examination be available.

SUMMARY

In most diseases there is a latent radiographic period between onset and radiographic signs. The latter do not coincide with the development of clinical signs but lag behind.

The interval between the appearance of clinical signs and the appearance of radiographic signs varies, not only in different diseases, but in different lesions and sites of these diseases. The clinical signs may have disappeared before the radiographic appear—the latter may persist to the end of the life of a healthy individual.

Obviously radiographs during the latent radiographic period will reveal no evidence of the disease though it may be present—further radiographs must be taken at an interval depending on the condition, if we wish to obtain confirmatory radiographic evidence. The interval between the first negative radiograph and the request for the second which shows positive signs is usually very much longer than the latent radiographic period—probably because the first radiograph was of a patient with prominent symptoms which have shown some abatement in the interval—the second only being called for because of a recrudescence of symptoms or a failure of the latter to clear within a reasonable time. The radiographic signs also lag behind and may even appear to increase after the clinical signs have disappeared, consequently we have to wait to obtain radiographic evidence of the effect of any treatment. Finally a clinical examination is an essential preliminary to any radiographic investigation.

Section for the Study of Disease in Children

President—HELEN M. M. MACRAY, M.D., F.R.C.P.

[March 23, 1945]

Meeting Held at the Queen Elizabeth Hospital for Children, London

Parenteral Infections in Gastro-Enteritis with Special Reference to Mastoiditis

By M. E. WEHNER, M.B.

THE cases which have been shown are those of gastro-enteritis with mastoiditis, and it was thought that it might be of interest to make a brief analysis of all the cases of gastro-enteritis admitted during the year 1944 with particular reference to any associated infections.

The analysis deals only with infants under 1 year of age who were either admitted with diarrhoea and vomiting, or else developed it in hospital. During the year there were 75 of these cases in the hospital of which 65 were admitted with diarrhoea and vomiting, and the remaining 10 developed it whilst in hospital for other reasons.

TABLE I.—AGE-GROUPS SHOWING MORTALITY AND DEHYDRATION

Age-group	No. of cases	Deaths		Dehydration	
		No.	Case fatality per cent.	No.	Per cent.
0-3 months	28	7	25	21	75
3-6 months	29	12	42.8	22	75.9
6-9 months	14	5	35.7	10	71.4
9-12 months	4	1	25	3	75
Total	75	25	33.3	56	74.6

A large proportion of the babies were under 6 months of age, the incidence of diarrhoea becoming much smaller towards 1 year of age. Only 3 of the patients were breast-fed, the others having been bottle-fed for varying periods.

As our isolation ward has only ten cubicles, only those children who were severely ill were admitted, the milder cases being treated as out-patients. The end columns in Table I show the numbers of patients who were dehydrated in the various age-groups, the figure being practically the same in each group, that is approximately 75%. The dehydration varied from minor degrees of inelasticity of the skin to severe dehydration with profound collapse and shock. Most of the cases which were not dehydrated on admission were admitted because of the severity of the parenteral infection.

In an attempt to determine whether an enteral infection was present, rectal swabs were taken, and in only one case was a pathogenic organism isolated; this being a case of Sonne dysentery which occurred during a minor epidemic. Further investigation showed that 46 of the cases had some associated parenteral infection at the onset of diarrhoea.

Table II shows the numbers of the various types of parenteral infections encountered.

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In an attempt to determine whether an enteral infection was present, rectal swabs were taken, and in only one case was a pathogenic organism isolated; this being a case of Sonne dysentery which occurred during a minor epidemic. Further investigation showed that 46 of the cases had some associated parenteral infection at the onset of diarrhoea.

Table II shows the numbers of the various types of parenteral infections encountered.

TABLE II.—PARENTERAL INFECTION WITH MORTALITY.

Associated disease	No. of cases	Dehydration	Deaths	Per cent. deaths
Mastoiditis	11	11	4	32.6
Suppurative otitis	9	7	1	
Pneumonia	10	6	5	
Pneumonia and otitis or mastoiditis	3	3	2	
Otitis—no pus	3	3	0	
Upper respiratory infection and bronchitis	7	5	3	
Furunculosis	2	1	0	
Pyelitis	1	1	0	
Total parenteral infection...	46	37 = 80.5%	15	32.6
No associated infection at onset of D & V. ...	29	19 = 65.5%	10	34.5

Many of the parenteral infections were of an extremely severe nature, some of the children having a double infection as well as the diarrhoea.

In 29 of the cases there was no associated infection found at the onset of the diarrhoea or when the patient was admitted, but some of these cases developed pneumonia and other infections later. It was thought that some of them had a parenteral infection, as the temperature remained high, and in some the ear drums were injected; but myringotomy revealed no pus, and no other focus of infection could be found.

All the cases were treated on the same general lines, and apart from a few details the treatment differed very little from that used in other hospitals. Sulphonamides were used, where necessary, for parenteral infections, but were not used for the gastro-enteritis alone except in 3 cases where sulphaguanidine was used. In the cases of otitis, sulphonamides were never given before a myringotomy had been performed.

Mastoidectomy was performed in 15 cases in 12 of which pus was found. Where no pus was found the wounds were sutured with no drainage. Gas and oxygen anaesthesia was used in all cases except one. In the latter case the baby was in a very poor condition and cyanosed, and local anaesthesia was used. 8 of the cases in which pus was found survived, and all these showed great improvement during the first week after operation. In 3 cases the improvement being marked as early as the second day, with cessation of vomiting, amelioration of diarrhoea, the temperature becoming normal, and progressive gain in weight.

Table I shows that the highest mortality was amongst the 3 to 9 months groups. Column 3 in Table II shows the deaths in relation to the various types of infection.

Of the 11 cases with mastoiditis alone 4 died. 2 of these developed pneumonia after the mastoid infection had begun to clear, while the other 2 failed to show much improvement after the operation and died within a week.

The fatal case with otitis media and diarrhoea was a baby who was moribund on admission and died within eight hours. Pus was found in the middle ear at post-mortem.

5 of the 10 cases of pneumonia died. In 2 the diarrhoea cleared up at least a week before the patients died, and the children finally succumbed to the pneumonia, which in one case was associated with multiple lung abscesses, and in the other with septicæmia. The 2 cases which had pneumonia and otitis on admission associated with the diarrhoea, both gradually went downhill and died.

Of the 3 deaths in the babies with diarrhoea associated with upper respiratory infections, one was found to have pertussis, one developed pneumonia, and the other was a very weakly baby which was premature at birth.

Of the cases in which there was no parenteral infection at the onset of diarrhoea there were 10 deaths, giving a % mortality of 34.5 as opposed to 32.6 for the parenteral infections. This is surprisingly high considering that these infants had none of these other serious associated infections as well as the diarrhoea. On further analysis of these cases, however, it was found that one was a Mongol which was admitted with diarrhoea and vomiting but developed pneumonia in hospital from which it died. Another was a case of congenital heart disease admitted for treatment of serious cyanotic attacks. This baby developed a mild diarrhoea whilst in hospital which cleared a week before it finally died during a cyanotic attack. At post-mortem this baby was found to have a gross congenital cardiac defect. A third case was found at post-mortem to have porencephaly. Another of these cases was admitted in a moribund condition and died twenty minutes after admission. The other 6 cases all pursued a gradual downhill course, with relapses and remissions, and died three to nineteen days after admission.

This brief outline of cases admitted during one year serves to show the importance of parenteral infections in relation to diarrhoea, and the serious prognosis, especially in those cases secondary to mastoiditis or pneumonia.

Dr. B. Cohen: I would like to deal shortly with the problem of diagnosis of middle-ear infection in these cases. Firstly, it must be stated that a normal drum precludes any mastoid or middle-ear involvement and conversely if pus is found in a mastoid at operation where the drum was considered to be normal, the error has been in otoscopic examination. If normal drums can occur with mastoid infections every case of gastro-enteritis would be a candidate for mastoidectomy. Secondly, the course of the infection in the middle-ear cleft follows fairly closely that of a similar subacute infection in older patients and it is only by repeated examinations of the drum-heads, from the time of admission, that an early and accurate diagnosis can be reached. Thirdly, in late cases, e.g. about the fifth to sixth week, the correct procedure should be mastoidectomy not myringotomy. Lastly, the instance of middle-ear infections in gastro-enteritis is sufficiently high to warrant more careful attention being paid to this problem.

Our figures for the period 1941-44 reveal that of 274 cases under consideration 68 had a middle-ear cleft infection; of these 28 had otitis media with 79% recovery following myringotomy and 40 mastoiditis with a 70% recovery rate.

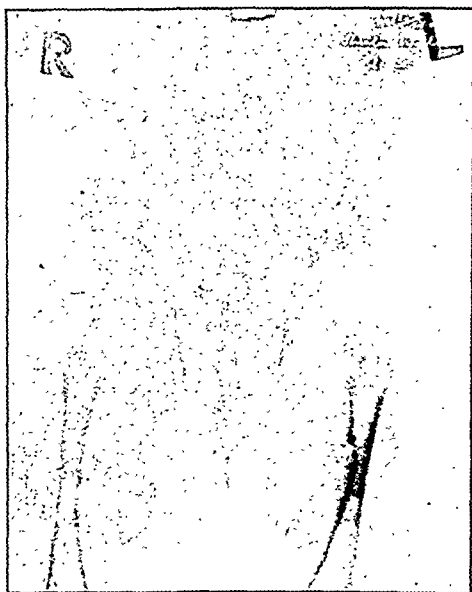
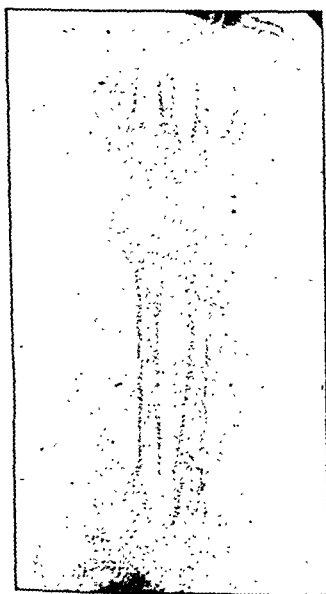


FIG. 1.

FIG. 1.—20.4.40: Aged 2 years 1 month. Forearm: extreme rarefaction, moth-eaten appearance of shafts of bones, fracture of ulna. No evidence of healing in spite of therapy with cod-liver oil, radiostoleum and ultraviolet light.

FIG. 2.

FIG. 2.—2.5.40: Aged 2 years 1 month. Pelvis and femora: extreme rarefaction, marked deformity of pelvis, fracture of left femur. No evidence of healing.

Rickets Resistant to Vitamin D; Healing with Very Heavy Dosage of Vitamin D, Fluctuations in Vitamin D Requirement, Development of Toxic Symptoms, and of Non-Rachitic Changes in Bones.—HELEN MACKAY, M.D., AND Q. I. MAY, M.B.

S. W., female, aged 7 years, born 29.3.38.

Family history.—Adopted at 8 weeks old. Nothing known of parents, except that patient first child of mother.

Patient's history.—Feeding in infancy: Sweetened condensed milk and barley water. Cod-liver oil said to have been given regularly from 8 months old. From 4 months to 18 months old suffered from fits (? tetany).

At 18 months old admitted to Queen Mary's Hospital, Carshalton. Colour good and well covered. Teeth malformed and carious. Rickets of extreme severity: square head, narrow chest, marked dorsolumbar kyphosis, enlarged epiphyses. No evidence of coeliac disease or renal disease. Radiograms: Very severe rickets, extreme degree of osteoporosis, shafts of bones looking "moth-eaten"—fractures of long bones and of ribs. From 18 months to 25 months old treated with cod-liver oil, radiostoleum, ultraviolet light therapy and calcium gluconate with no improvement in bones. Blood chemistry: Serum Ca 7.2 mg. per 100 c.c.; serum inorganic P 2.85 mg. per 100 c.c.; phosphatase 110 units (King



FIG. 3



FIG. 4.

FIG. 3.—10.7.40: Aged 2 years 3 months. Forearm showing early stage of healing on 150,000 I.U. of vitamin D daily. Moth-eaten appearance of shafts of bones is well shown.

FIG. 4.—11.9.40: Aged 2 years 5 months. Forearm showing fairly advanced healing on 250,000 I.U. of vitamin D daily.



FIG. 5.

FIG. 5.—13.3.44: Aged 6 years. Femora showing defects in ossification: pseudo-crack at lower end of right femur and ovoid area of deficient calcification in shaft of left femur.

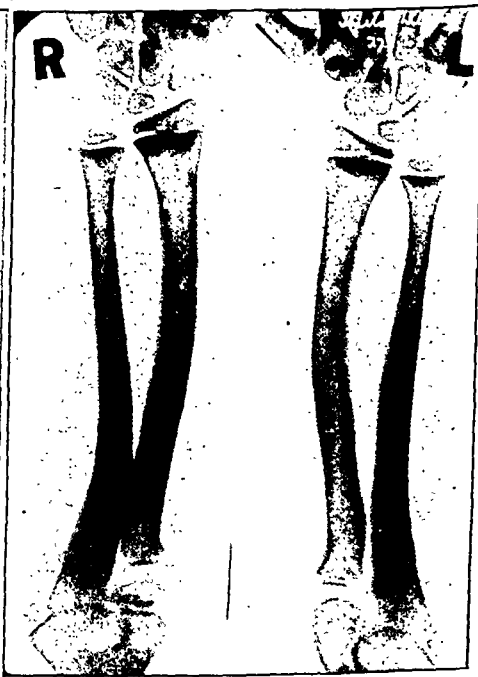


FIG. 6.

FIG. 6.—27.1.45: Aged 6 years 10 months. Forearm showing bones completely healed.

and Armstrong) per 100 c.c. On account of kyphosis treated on "frame", which produced antero-posterior flattening of thorax. At 25 months old given 100,000 I.U. of vitamin D intramuscularly—no change in radiograms after three weeks.

From 2 years and 1½ months to 2 years and 7 months old treated with vitamin D by mouth in increasing dosage. Early healing on 150,000 I.U. (Ostelin tablets) daily, advanced healing two months later on 250,000 I.U. daily. Serum Ca rose to 12.0 mg. and serum inorganic P to 4.2 mg. per 100 c.c. From 2 years and 7 months to 2 years and 10 months old, evacuated—no vitamin D given after first few weeks—returned to hospital with active rickets. From 2 years and 10 months to 4 years and 3 months old: Very slow healing in five months on 250,000 I.U. daily, and dose therefore gradually increased to 450,000 I.U. daily. Rachitic lesions healed completely, but non-rachitic disturbances of ossification became apparent at the lower end of the femora: a large "island" of deficient calcification in the shaft of the left femur, a pseudo-crack extending obliquely through shaft and epiphyses with disorganization of ossification at the lower end of the right femur. Dose of vitamin D was reduced to 400,000 I.U. daily. From 4 years and 3 months to 5 years and 7 months, rickets remained healed, non-rachitic changes in femur persisted, and after fifteen months on 400,000 I.U. of vitamin D daily toxic symptoms suddenly developed, and dose was stopped for five weeks. From 5 years and 7 months to 6 years, and 10 months non-rachitic lesions in femur improved and rickets remained healed as judged by radiograms. After about three months on 50,000 I.U. of vitamin D daily the serum inorganic P had dropped and dose was increased to 100,000 I.U. daily which caused a rise of P to normal level. Child was transferred to the country branch of the Queen Elizabeth Hospital for Children. Her general health was good and she was running about easily until she developed a severe and persistent bout of vomiting with dehydration. No cause was found, and there was no hypercalcaemia, but the dose of vitamin D was reduced to 50,000 I.U. daily. She developed otorrhœa just before discharge from the ward.

Condition on discharge from ward at 6 years and 10 months old in January, 1945—Weight 3 st. 4½ lb. Child still pale and tired after her attack of vomiting, gait waddling, and stance poor. Stature small owing to her very short limbs: proportions those of a child with achondroplasia. Epiphyses at wrist still large and chest is flat, though its shape has greatly improved. There is marked anterior bowing of the femora. Right lower limb is ½ in. shorter than left.

Radiograms: Forearms—bones well calcified and rickets completely healed. Femora—appearance suggests some sclerosis at lower ends of bones, but these look much less abnormal than two years ago. Coxa vara present.

Present condition.—7 years old. Just back from a stay in the country and looks in good general health. Gait still waddling and very ungainly.

Rickets Resistant to Vitamin D: Healing with Very Heavy Dosage of Vitamin D, Fluctuations in Vitamin D Requirement, Development of Hypercalcaemia.—HELEN MACKAY, M.D., and Q. I. MAY, M.B.

J. L., aged 16 years, born 13.4.28.

Family history.—Father: treated for rickets till 20 years old, height about 4 ft. 6 in., severe bony deformities, one leg shorter than other. X-ray of forearm and leg shows broadening of lower part of shaft of radius and ulna and of head of fibula, probable old fracture of radius, marked osteoporosis of femur, tibia and fibula, bending of leg bones, extreme genu valgum. Mother: health good, stature small. Siblings: two brothers: one brother epileptic, no rickets. Other brother, aged 2 years, developed slight rickets at 6 months of age while having two teaspoonfuls of cod-liver oil daily, and rickets healed on four teaspoonfuls of cod-liver oil compound (about 2,800 I.U. of vitamin D) daily. Maternal uncle: epilepsy. Maternal aunt: asthma.

Patient's history.—Birth weight 5 lb. 1½ to 4 years old treated for rickets at Westminster Hospital and at welfare centre. Attacks of asthma. At 4 years of age sent to Queen's Hospital by Dr. E. McGregor. Weight 29 lb., short-limbed child with active rickets and bronchitis, coxa vara and slight genu valgum present. Teeth good. No evidence of renal disease or of defective fat absorption.

From 4 to 9 years old, treated with cod-liver oil, radiostoleum and ultraviolet light. This appeared to keep rickets in check—sometimes there was advanced healing of the rachitic lesions, only to be followed by relapse. Child often complained of pain in legs. The degree of rachitic change at the two wrists was not identical. Dr. R. A. McCance suggested and tried intramuscular injection of glycerophosphate, but without benefit. Serum Ca remained at normal level, and serum inorganic P remained persistently low at 2.5 or 2.6 mg. per 100 c.c. During this time child had occasional attacks of asthma, also measles, scarlet fever and about six epileptic attacks.

From 9 to 12 years old, treated with gradually increasing dosage of vitamin D (ostelin tablets). Advanced healing on 500,000 I.U. daily, complete healing and hypercalcaemia with 600,000 I.U. daily at 12 years old in 1939. Toxic symptoms with hypercalcaemia have occurred at different times and have been: anorexia, nausea, vomiting, "giddy feelings", headache, abdominal pain, pain in flank, dysuria, frequency of micturition and sharp loss of weight, sometimes accompanied by "calcium casts" in the urine. On one occasion when the serum Ca rose to 16 mg. per 100 c.c. the blood urea rose to 76 mg. per 100 c.c., but dropped to 24 mg. per 100 c.c. within a few days of stopping vitamin D. Child evacuated with her school for physically defective children at outbreak of war and was given no vitamin D for seven months: had much pain in legs and was kept in bed. Brought back by mother with active rickets. From 12 to 14 years old, treated with vitamin D, gradually increased to 550,000 I.U. daily, with return of hypercalcaemia before rachitic lesions healed. Later dose increased to 600,000 I.U. daily. Rickets not completely healed again till 13½ years old. General health good during most of this period, but had appendicitis. Between 14 and 16½ years old, two further attacks of hypercalcaemia with toxic symptoms, and on other occasions hypercalcaemia without toxic symptoms, hence vitamin D gradually reduced to 12,500 I.U. daily.

Present state.—Age 16½ years. Weight 8 st. 2 lb. 13 oz. Height 4 ft. 7 in. General

health good, but gets "aching of thighs". Intelligence good. Proportions those of a patient with achondroplasia: trunk and head of normal size with short limbs and waddling gait. Shape of chest normal. Costochondral junctions and epiphyses at wrist enlarged. Femora bowed, convexity forwards, coxa vara present. Left lower limb shorter than right by half inch. Teeth: slight hypoplasia, some stoppings.

Radiograms: Bones well calcified and rickets healed fully. The "island" of deficient calcification in the shaft of the right radius which has been present since the age of 6 years is now very much smaller.

Comment.—Since Albright and his colleagues published in 1937 their description of the cure of a boy with rickets resistant to vitamin D therapy with heroic dosage of vitamin D (their maximum dosage was $1\frac{1}{2}$ million units daily), there must have been many cases treated with enormous doses, though not very many have been published. Highman and Hamilton in the previous year came near to discovering how to cure cases of this type when they showed the beneficial effect of 100 drips of viosterol daily. The nature of the inherited defect causing rickets in these cases is not known. It has been shown that, as in ordinary rickets, there is hyperplasia of the parathyroids, a low level of inorganic phosphorus in the serum and diminished output of calcium and of phosphorus in the urine in the active phase, and under treatment with massive doses of vitamin D, Eliot and Park (1944) have shown that the vitamin D in the blood reaches extraordinarily high levels. One point that is brought out clearly by our case is the fluctuation in the need of vitamin D: a dosage bringing about rapid cure at one stage, may prove insufficient at another, and perhaps more serious, a dose that has been well tolerated for as long as fifteen months may suddenly cause toxic symptoms necessitating immediate stopping of the drug. I suggest that everyone advising this massive therapy should be alive to this danger and children so treated should be examined at regular intervals and that mothers should be told to stop the drug if toxic symptoms develop. J. L. has required progressively smaller doses since puberty, and perhaps when she ceases to grow she may not require further treatment. The Council of Pharmacy and Chemistry in the United States (1943) has issued a warning that operative procedures to correct deformities in children under massive dosage may precipitate toxic symptoms; it seems that immobilization from any cause may induce hypercalcaemia (Eliot and Park, 1944).

J. L. and her brother and S. W. are examples of differing grades of the disease—B. L. very mild, S. W. extremely severe. The extraordinary "moth-eaten" appearance of the shafts of the bones of S. W. when first seen made one consider renal rickets. J. L. and her father and S. W. all show some bone change other than the rachitic lesions; and each has one leg slightly shorter than the other, perhaps due to the rachitic lesions not being of quite equal grade in the two limbs. I wondered whether the abnormal ossification at the lower ends of the femurs of S. W. could be attributable to overdosage of vitamin D and hypercalcaemia but the lesions do not suggest those of osteitis fibrosa with hyperparathyroidism.

Mr. H. A. T. Fairbank has shown me radiograms of school children with persistent rickets very likely of this type and several have areas of rarefaction or other abnormalities of ossification in the long bones. Christensen (1941) says that in his cases there were, in addition to rickets, bone changes somewhat resembling those found in Morquio's disease. In any case both in Christensen's cases and in ours the residual lesions in the bones have gradually improved.

J. L. is at times troubled by "aching in the thighs." We should be glad of advice as to whether anything can be done to alleviate this, and whether osteotomy of the femora is indicated for S. W.

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Glioma of The Optic Chiasma.—MAJOR J. MINTON. I was asked to see this patient two weeks ago with the view of removal of the right eye which became extremely proptosed. I found both eyes blind and markedly proptosed and also deviated downwards and outwards, the right eye much more so than the left.

On 8.3.45 before the excision of the right eye I examined both fundi under an anaesthetic. The corneae and media of both eyes were clear and the fundi could be seen easily.

The fundus of the right eye.—A grey tumour, the size of the disc, was seen on the outer and upper side of the disc between nine and twelve o'clock. The tumour was about five diopters high with the vessels curving over it. The disc was grey with no sign of papilloedema.

The fundus of the left eye.—A greyish disc was seen with indefinite edges. The rest of the fundus was normal.

At operation for excision of the right eye, the optic nerve was found to be surrounded by a large encapsulated tumour, ovoid in outline and larger than the eyeball. The tumour was freely detached from the surrounding orbital tissue, but its posterior limits could not be defined as it seemed to be coming from the anterior cranial fossa.

The eye with its adherent mass was removed. The specimen was sent for microscopical examination. This is most probably a glioma of the optic chiasma which is growing through the optic foramina into both orbits.



Glioma of the optic chiasma growing into both orbits.

Hyperplasia of Gums with Epanutin Therapy. Two Cases.—A. I. DATE, M.B.

There are a few points about these two cases which are of interest.

Both boys have been given the same dose of epanutin, i.e. $1\frac{1}{2}$ grains t.d.s. combined with luminal. In Case 12 the first sign of hyperplasia was noticed after sixteen months under treatment. In Case 11 the exact date of onset is not known but the condition was marked after thirteen months of treatment.

This condition of hyperplasia of gums is not an uncommon accompaniment of epanutin therapy and has been reported since 1938 by various American and British authors, the first reports coming from the U.S.A. where the drug is used under the name of Dilantin. The percentage of cases affected has been stated to be as high as 55 to 68% by different observers.

The overgrowth of gum tissue appears to be a true hyperplasia (not a hypertrophy) and as it has not occurred in edentulous patients it is thought to arise in the periodontal tissue. Characteristically the growth is of normal colour, painless, and with no tendency to bleed.

It would appear that the hyperplasia is a toxic manifestation, but it does not seem that its occurrence is directly related to the dose of drug used, the length of treatment, or the age of the patient.

Other toxic symptoms reported in cases treated with epanutin are: Nystagmus, diplopia, vertigo and ataxia, mental irritability and confusion, fatigue and apathy, nausea and vomiting, and less commonly cutaneous eruptions. So far none of these has been observed in our two patients.

The diagnosis must, of course, be made from other conditions causing generalized swelling of the gums in children, namely, chronic inflammation, usually associated with mouth-breathing; vitamin C deficiency; congenital (or hereditary) hyperplasia. The latter bears the closest resemblance clinically to epanutin hyperplasia, but it commonly occurs at the time of dentition. The other two conditions can be excluded by the absence of pain and tendency to bleed.

It has been claimed that the hyperplasia tends to disappear on withholding the drug but in view of its great advantages over luminal and other drugs in selected cases of epilepsy, this measure is rarely contemplated unless more unpleasant symptoms are present. In our two cases the question was considered and it was decided that the dramatic success obtained with epanutin in both cases fully justified continuing its administration. In this opinion we were supported by Dr. Tyler Fox of Lingfield epileptic colony where Case 11 lived for several years and where his treatment with epanutin was started.

The possibility of resection of the redundant gum tissue has also been considered and decided against, as, according to present reports, it is likely to be followed by recurrence with increased rate of growth.

Careful supervision of these cases is of course essential, and a close watch should be kept for early neurological or other toxic manifestations. Oral hygiene and regular dental supervision are no less important.

Congenital Bilateral Megalo-ureters with Hydronephrosis: A Remarkable Family History.

—HELEN MACKAY, M.D.

H. M., female, aged 4½ years.

Family history.—No consanguinity of parents. Father died of cerebral hæmorrhage. Mother alive: apparently toxæmia during all pregnancies. Patient 7th child in family, 1st and 3rd siblings alive and well, but one has megalo-ureters; 2nd, 4th, 5th and 6th siblings stillborn or died in early infancy, two with sarcoma of kidneys, one with hydronephrosis (in this hospital), one cause of death unknown. (Dr. G. S. B. Phillips has kindly supplied details as to the stillborn children.) Paternal grandfather had nephrectomy for calculous pyonephrosis (see family tree).

Patient's history.—Date of birth 26.6.40. Birth-weight 8 lb. 15 oz. Good progress till 9 days old, thereafter vomiting and loss of weight. Attended Queen's Hospital for Children from 11 days old. Vomiting lasted till about 4 weeks old, gain in weight irregular till 2 months old, thereafter and until present time general progress has been satisfactory. Fracture of left parietal bone at 11 months old.

Pathological examinations.—Urine: No abnormalities found at any time, except at 11 months old when there were a few red cells and pus cells and casts on one occasion.

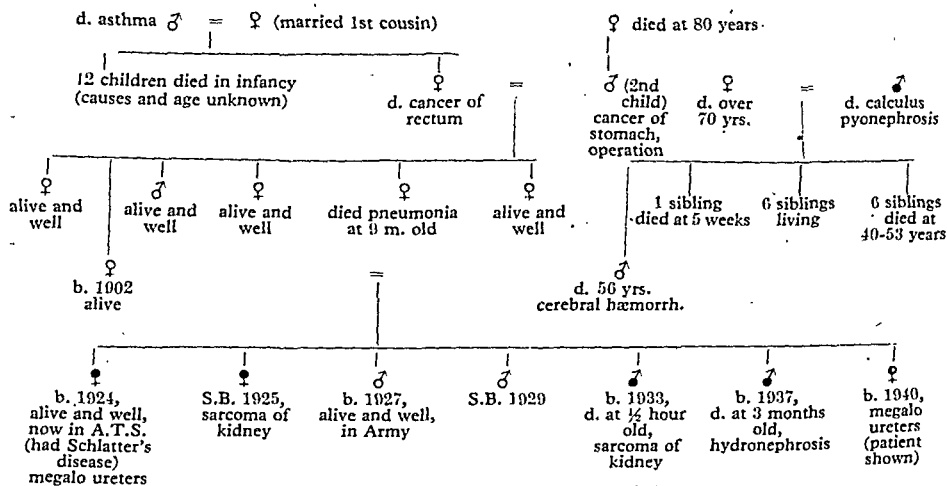
Blood urea in mg. per 100 c.c.

Age:	13 days	20 days	1½ m.	1¾ m.	7 m.	11 m.	12½ m.	1½ y.	2 y.	3½ y.
Blood urea:	100	126	50	63	35	38	64	32	20	26

Child was not dehydrated at 20 days old when blood urea reached its highest level. Radiograms: At 24 days old film taken two minutes after injection of 8 c.c. of uroselectan into left external jugular vein showed gross dilatation of both ureters and some hydronephrosis: no delay in excretion. (This dose of uroselectan caused immediate vomiting.) At 1½ months 4 oz. of sodium iodide solution (13.5%) injected into bladder: no fluid entered ureters, and emptying of bladder appeared normal. At two years old intravenous pyelogram repeated: ureters appear very much less dilated.

Present state.—Age 4½ years. Weight 2 st. 9½ lb. Height 3 ft. 6 in. General health and development satisfactory, but tonsils and tonsillar glands are enlarged.

Urine: n.a.d. Radiograms of long bones: n.a.d.



Discussion.—In this family of 7 siblings, 5 are known to have had congenital lesions of the kidney or ureter—3 had megaloureters (two bilateral) and two congenital sarcoma of the kidney. The mother was attended by Dr. G. S. B. Phillips and the diagnosis of sarcoma was, he informs us, established by examination of microscopic sections in a well-known laboratory. It is difficult to see what possible connexion there can be between the two types of lesions, so I presume their co-existence in the same family must be put down to coincidence. The paternal grandfather died with a pyonephrosis, so may have had a congenital hydronephrosis.

The child shown was thought to be suffering from uræmia in the neonatal period (with vomiting and a blood urea level of 126 mg. per 100 c.c.) but to my surprise now at 4 years old she seems quite normal in health and development. The child was not dehydrated at 20 days old when the highest value for blood urea was obtained, and though high values are known to occur in the neonatal period a figure as high as this is surprising.

Congenital Deformities. Two Cases.—G. O. TIPPETT, F.R.C.S.

CASE I.—Male child born with defective upper limbs. On the left side the arm stopped short in the lower arm, the stump having a thumb and rudimentary digit as useless skin appendages placed on the lower inner aspect of the arm, whilst there was a complete absence of an upper limb on the other side. Though the clavicle on this side was developed, there was only a small osseous fragment representing the scapula. Lower down on the lateral chest wall there was a papilla in a depression, perhaps the attempt to form a limb bud.

CASE II.—Female child born with defective lower limbs. Both hips and knees were acutely flexed, whilst the ankles were in marked calcaneo-valgoid talipes deformity. The joints were normal, as were the muscles of the limb.

The cases were shown to demonstrate the abnormalities namely, intra-uterine amputation or suppression of limb buds at the worst, or soft part contractures at the best when the normal lie of the fetus is interfered with owing to amniotic bands, lack of fluid or tight umbilical cord, &c.

The following cases were also shown:

Cleft Lip and Palate Repair; Cases.—Mr. J. P. REIDY for Mr. T. POMFRET KILNER.
 Bladder Neck Obstruction with Acute Retention and Cystitis; Two Cases.—Mr. H. P. WINSBURY-WHITE.

Still's Disease with Dislocation of the Hip.—Dr. C. T. POTTER.

Chronic Military Tuberculosis.—Dr. C. T. POTTER.

Pseudohypertrophic Muscular Dystrophy.—Dr. HAROLD AVERY.

Pulmonary Abscess treated with Penicillin.—Dr. J. N. O'REILLY.

Schizophrenia in a Boy of 7 Years.—Dr. URSULA JAMES.

[April 27, 1945]

DISCUSSION ON PENICILLIN IN THE TREATMENT OF DISEASE
IN CHILDHOOD

Mr. Ian Aird [Abridged]: When a new remedy becomes available, we must by patient and detached observation avoid the almost inevitable early over-optimism, and the equally inevitable reaction of disappointment which follows it. In introducing penicillin in the treatment of children, it is our responsibility (1) to ensure that, in all the cases we assess, the clinical diagnosis is accurate and supported by bacteriological evidence not only of the organism responsible, but also of its sensitivity to penicillin; (2) to satisfy ourselves that the best available method of administration, dose and duration of treatment is employed for each particular age-period and each particular disease; (3) to supplement penicillin administration with such ancillary therapeutic measures as may from time to time be found necessary, but to remember that variations in these may be responsible for variations in the effectiveness of penicillin. It is further our duty, and in the case of penicillin it has been a pleasant duty, to assess the benefit which penicillin confers by whatever standards of measurement we find available or can contrive—the fatality rate, the duration of individual symptoms and signs, the period during which organisms survive in the tissues of the patient's body, the date of recovery of function and the degree of function recovered, and the liability to relapse—comparing these data with our knowledge of the behaviour of the disease when treated by older methods. Finally, we have an opportunity of establishing the pathological course which is followed by a disease modified by penicillin therapy. I shall follow this scheme of clinical trial closely in the description of our experiences with penicillin in the treatment of acute osteomyelitis, which we have specially studied. My conclusions are based particularly on fourteen children suffering from this condition who have been treated in my own charge during the last year, but they are supported by the observations made by Dr. I. W. J. McAdam, and shortly to be published, on twenty-eight older patients of whom I have direct or indirect knowledge.

(a) *Diagnosis*.—For the precise diagnosis of acute osteomyelitis we have introduced routine marrow puncture. In obvious or suspected osteomyelitis, under local or general anaesthesia, a sternal puncture needle is introduced into the marrow, close to the primary seat of the infection, in the metaphysis of the infected bone. This procedure is particularly simple when, as in the tibia, the metaphysis presents a subcutaneous surface. The needle, with stylet in place, is made to pierce the skin and the firm cortex (often softened by inflammation) until resistance ceases and the point lies in the unresisting medulla. Even such a deeply buried metaphysis as that of the neck of the femur offers no difficulty; the needle is introduced just below the trochanter, along the line of the neck as determined from the straight X-ray; in the child, the anterior aspect of the rim of the head can be palpated from the femoral triangle, and the palpating fingers over it are a guide for the depth of the plane in which the needle lies; the procedure is infinitely simpler than the introduction of a guide wire into the fractured neck of an old lady's femur, and the intracervical situation of the point can always be verified by stereoscopic plates.

Marrow puncture has been performed in all the patients of my series, so that cases of bone pains which, subsiding spontaneously even in the days before penicillin, were sometimes rather loosely labelled mild osteomyelitis, are not included in our assessment. Puncture has always provided either a sanguineous fluid with flakes of pus floating in it, or a frankly purulent exudate under considerable tension. In every case *Staphylococcus aureus* has been grown from the fluid obtained.

We have found these benefits in marrow puncture: (1) accuracy is obtained in bacteriological diagnosis even if blood culture is negative; (2) the penicillin sensitivity of the organism can be determined, and a precise prognosis furnished; (3) tension is relieved near the centre of infection; (4) an additional route (local intramedullary) for penicillin administration is available should it be desired; and (5) if the needle is left in place and repeated specimens of pus are aspirated, the time of clearance of organisms from the bone-marrow, and the required duration of penicillin administration can be precisely determined in every case.

Aspiration of marrow for diagnosis and control of treatment in osteomyelitis is analogous to the urethral smear in urethritis.

(b) *Methods of administration*.—The repeated injection of penicillin we abandoned because of the increasing horror with which the children awaited each succeeding injection. While we had general satisfaction thereafter from the continuous intramuscular method of penicillin administration, we were impelled by reasons which have little importance now to seek an alternative route, and we decided to test the direct continuous intramedullary instillation of penicillin by way of the marrow needle, from the Eudrip 3 apparatus of Duguid and McAdam. This method has been employed in twelve cases of infection of the long bones. By it, penicillin can be introduced painlessly over a period of three weeks or longer without intermission, without change of needle or change

of site, and without secondary infection. Numerous observations have shown uniformly not only a concentration of penicillin of the order of 1:1,000 at the site of the lesion, but a constant blood level no less than that obtained by the intramuscular method. If perabrodil is injected along the intramedullary needle, it is found to pass freely through the intercommunicating abscesses of the marrow to reach rapidly the subperiosteal space; we have not only a satisfactory blood level, but a generous local pool of penicillin.

It is not suggested that this intramedullary method should be regarded as standard in osteomyelitis. As in intramedullary saline infusion, the rate of acceptance of the fluid is slow initially, and a suitable speed is reached sometimes only after a few hours of accelerating flow. Moreover, in isolated cases when instillation has been continued for more than a fortnight, a sinus has persisted for a week or two at the site of needling. The method has, however, certain advantages: (1) A high local concentration of penicillin is obtained without loss of blood concentration; (2) only the diseased limb need be immobilized; when the intramuscular method is used, and the needle alternates from limb to limb as it must in young patients, the diseased extremity and the penicillin receptor require simultaneous immobilization with consequent increase in nursing difficulties; (3) in infection of such sites as the upper femur, with concomitant joint involvement, a high local concentration of penicillin in the infected joint is presumed; (4) in young children, with small and perhaps wasted muscles, when intramuscular administration evokes swelling and pain, the intramedullary route is kinder.

One problem of administration remains to be solved. We are not satisfied that the intramuscular method as used at present is suitable for very young infants. Whether the continuous drip be employed or the method of repeated injection, abscesses seem to be almost inevitable at some at least of the injection sites. These abscesses have proved sometimes to be sterile, sometimes to be infected with coliform bacilli or even penicillin-sensitive staphylococci. The cause of abscess-formation in these infants is still uncertain. Important may be the small bulk of the muscles, the sensitivity of young muscle to chemical irritation, and surface infection by organisms from the napkin area. We have made a practice of immobilizing the lower extremities of young infants by suspension from a gallows frame to ease nursing and reduce faecal contamination of the thighs; we reduce the dose of penicillin and the volume of injected fluid to the lowest possible level; and we choose for infants those proprietary forms of penicillin which seem to be purest and most free from irritant effects: even so, injection abscesses continue, and the only death in my own series has been that of an infant with polyarthritis who developed multiple abscesses while under penicillin treatment. Because of the risk of secondary infection we have not used the intramedullary method in infants.

(c) *Supplementary procedures.*—When penicillin is given for long enough in adequate concentration, we find no necessity for radical surgery. In my own cases, treated conservatively, sequestrectomy has never been required, nor has persistent suppurative or sinus-formation occurred. Our surgical intervention has been limited to needle aspiration of the metaphyseal focus at the commencement of treatment, except in two cases, in each of which a subcutaneous abscess required simple drainage at a late stage of the disease, some weeks after its onset. These abscesses presented no communication with the bone, and furnished only a quantity of clear fluid with golden crystals floating in it. In one instance the fluid was sterile, from the other, penicillin-sensitive *Staphylococcus aureus* was cultured. In the latter case, the marrow had previously been shown to be sterile, the abscess healed after drainage, and complete recovery to an ambulant stage followed in a fortnight; the subcutaneous abscess had persisted when the intra-osseous abscess had healed.

In all our patients, the affected limb has been immobilized as completely as possible for so long as it has remained swollen and tender—usually for a week or two after penicillin is stopped. In infection of lower femur and tibia, plaster has been employed for immobilization. Upper femoral infections have been treated by extension in a Thomas' splint. Plaster has been used for infection of the bones of the upper extremity.

In general I am satisfied that the standard treatment of osteomyelitis should include (1) needling of the metaphyseal focus for bacterial diagnosis, sensitivity tests, and relief of tension (the subperiosteal space may be emptied by aspiration at the same time); (2) continuous distant intramuscular penicillin instillation, maintained until the marrow is shown, by repeated metaphyseal aspiration, to be sterile; (3) immobilization; and (4) the simple drainage of subcutaneous abscesses. Our intrametaphyseal route for penicillin administration may be reserved for poorly nourished children to whom the intramuscular method gives pain, and for certain special situations, such as the hip, perhaps, where the joint is concomitantly involved.

(d) *Standards of benefit.*—(1) *Fatality rate:* Great care must be taken in the estimate of fatality rates in acute osteomyelitis. The disease varies greatly in severity from time to time, and our data are insufficient for a statistical analysis. Sometimes years pass in our hospital without a death, and then we have a minor epidemic with a high fatality rate. Yet the results we have seen have been so dramatic—delirious patients recovering

in a few weeks and ambulant with their lesions healed in a few months in spite of a positive blood culture, multiple foci of osteomyelitis, and even suppurative pericarditis—that the value of penicillin in the acute septicæmic form of osteomyelitis seems to be proved. In my series of 14 cases, supplemented by McAdam's 28 cases at older age-periods, 20 patients have provided a positive blood culture; there have been two deaths. In one of these, the causative organism was known to be penicillin-resistant. The other was the young infant with staphylococcal polyarthritides, whose death at 5 weeks from multiple abscesses has already been mentioned. Penicillin may well be regarded as a specific cure for septicæmia due to penicillin-sensitive staphylococci, except in extreme infancy. Let us hope that the last qualifying clause can soon be omitted.

(2) Delirium: Three of our 14 children were delirious when first seen. All these emerged from delirium after three to four days of treatment.

(3) The temperature is slow in responding to penicillin treatment and returns gradually to normal only after some days. An initial fall to normal on the first or second day of treatment is not unusual, and is always transient. The temperature sometimes rises towards the end of the third week of treatment, but usually falls to normal again abruptly when the penicillin is stopped.

(4) Blood culture, if positive before the beginning of treatment, invariably proves sterile five days after the beginning of treatment, and frequently earlier still.

(5) Metaphyseal infection: By withdrawing daily specimens of pus from the infected marrow by way of an indwelling intramedullary needle, it has been shown that the marrow cavity becomes sterile in eight to twenty (average fourteen) days, whether penicillin is given by the local intramedullary or the distant intramuscular route.

(6) Leucocyte count: The white count begins to fall much later than the temperature. Indeed, the leucocytosis diminishes only after the infected marrow is cleared of organisms. If metaphyseal puncture were not employed to govern the duration of treatment, a falling white count might be taken as an index of marrow clearance, and as a sign that penicillin might safely be discontinued.

(7) Swelling and tenderness: These have sometimes continued for some weeks after cessation of treatment, swelling outliving tenderness.

(8) Return of function: Weight-bearing has not been permitted until substantial reconsolidation is radiologically obvious in the diseased bone. After osteomyelitis of the tibia, weight-bearing has been permitted as early as five weeks, and the patient has shortly afterwards been satisfactorily ambulant. After infection of the upper femur, weight-bearing has been necessarily postponed until twelve to sixteen weeks or even more after the onset of the disease. The dangers of early weight-bearing are real; I know of one instance in which pathological fracture of a humerus was occasioned by too-early movement in bed.

(9) Complications: In my own patients, such distant complications as renal infection and lung infection have resolved under general penicillin treatment. Suppurative pericarditis has not occurred in my personal series, but in one patient of Professor Learmonth's whom I had an opportunity of seeing, and who suffered from a blood infection and general osteomyelitis, a suppurative pericarditis healed completely with repeated aspiration of pericardial pus, and penicillin replacement, concurrently with generalized penicillin administration.

Of the local complications, suppurative arthritis has been the most serious. My own series includes three cases of suppurative arthritis of the hip proved by puncture. All of these recovered. Two obtained a return of full movement at the hip, and were walking perfectly after twelve and sixteen weeks respectively. In the third case, healing was by ankylosis, and the child is now walking well ten months after onset of the disease. In the previous 9 cases of suppurative arthritis of the hip treated before penicillin in the same charge, 4 died, 4 still require treatment from time to time two to four years after the onset of disease, and only one spent less than eighteen months in a hospital bed.

(10) Relapse: Recurrence has not yet occurred in our series, and our evidence of marrow sterility is so conclusive that we do not expect it. It is well to remember, however, that formerly relapse was a common feature of osteomyelitis, and we have hardly had time to see it yet.

(e) *The course of the disease as altered by penicillin.*—Our conception of the pathology of acute osteomyelitis modified by penicillin administration depends on marrow puncture in the initial stages of the disease, and, later, on the radiological appearances. Marrow puncture shows clearly that organisms disappear from the metaphysis some fourteen days after the commencement of treatment. Only at this time, or a little before it, do X-ray signs of bone disease appear. The initial sign of an area of translucency

in the metaphysis appears now as it did in prepenicillin days. With it there is a thin line of subperiosteal new bone. This new subperiosteal layer, however, increases little in thickness, and a dense involucrum is exceptional. Decalcification proceeds, however, and the shadow of the bone architecture is lost. There is a curious time lag between infection and radiological appearances, and decalcification is maximal some weeks after all infection has disappeared from the marrow. The lack of the dense shadow of a thick involucrum exaggerates the translucency of the shaft, and an infected bone treated by penicillin looks more tenuous and ghostly than an infected bone which is allowed to proceed through its natural and unmodified pathological course. We merely see more clearly now the radiological appearances which were present in the infected bones in the old days, but were then masked by the density of the surrounding involucrum. Decalcification seems to be a necessary sequel of bone infection, even when infection is shortlived. Whether the bone lamellæ disappear to be temporarily replaced by granulation tissue, or whether the lamellar structure remains, merely losing its calcium salt, must be a matter of conjecture; yet the reappearance of a normal architecture, completely calcified, sometimes occurs so soon—within two months of complete decalcification—that one is forced to the conclusion that the process of rarefaction is one of decalcification of lamellæ which are themselves left intact.

Sequestrum formation has been almost entirely absent in my series. In one case of osteomyelitis of the tibia a tiny sequestrum appears to have formed, so small that absorption seems likely, and surgical interference unnecessary. Massive sequestration of infected bone has been reported in the literature of the penicillin treatment of osteomyelitis, but appears to have occurred only when general penicillin administration has been supplemented by extensive local intervention on the infected bone.

In giving this paper I have been only the mouthpiece of a team of workers under the general direction of Professor J. R. Learmonth. The bacteriological investigations were performed in the Bacteriology Department of Edinburgh University (Professor T. J. Mackie). Most of the clinical details have been superintended by Dr. I. W. J. McAdam, the bacteriology by Dr. J. P. Duguid. A part of the penicillin used was provided by the Penicillin Clinical Trials Committee of the Medical Research Council.

Dr. Martin Bodian [Abridged]: Dosage.—The problem of dosage of penicillin in infancy was investigated at the Hospital for Sick Children, Great Ormond Street, since February 1944, when the Penicillin Trials Committee allowed a small monthly quota of penicillin for this purpose.

It is generally known that penicillin is excreted rapidly by the kidneys in the adult and that traces only or no penicillin at all can be found in the blood three hours after an injection of the standard dose of 15,000 units. This applies equally to bigger children. It is also known that impaired renal function leads to prolonged retention of penicillin in the body. This observation has guided us in our efforts to space penicillin more widely in infancy, when renal function is not fully established.

Penicillin was given in four-hourly intermittent doses, mainly by the intramuscular route and the dosage calculated on the basis of 1,000 units per pound expected body-weight in twenty-four hours. The linking of dosage to the expected body-weight is an alteration of Florey's original recommendation for the treatment of infants, and so is the four-hourly spacing. The expected body-weight should be calculated from the birth-weight of the infant and its age. This is particularly important in dehydrated infants who need more penicillin than would be given them according to their actual weight. One has not aimed at mathematical precision in working out the dosage, but has chosen the nearest convenient round figure above the calculated dose.

Solutions were always made up in normal saline to contain one dose in 1 c.c., and injections made to coincide with feeding times which is an obvious advantage of the four-hourly intermittent spacing.

Nearly 200 penicillin estimations were carried out with serum of 57 infants to see whether this scheme of dosage was adequate. Adequate and not optimal dosage was what we aimed at, since penicillin was very restricted in supply. The penicillin levels were carried out by the modified slide method described by Garrod and Heatley [1] which is convenient for use in infants as it requires only 2 to 3 drops of serum.

Bacteriostasis at the end of three and four hours or even after three hours only was considered adequate enough a level in the great majority of cases.

TABLE I.—ANALYSIS OF 200 PENICILLIN LEVELS IN SERUM OF 57 INFANTS UNDER 1 YEAR, DAILY DOSE 1,000 UNITS PER POUND EXPECTED BODY-WEIGHT FOUR-HOURLY I.M.

Interval after injection	Number of samples with inhibition powers up to dilution of				
	1 : 1	1 : 2	1 : 4	1 : 8	
4 hours complete bacteriostasis	26	5	1	2	Group I Complete bacteriostasis after 4 hours
	Total 34 cases (equals 60%)				
4 hours partial bacteriostasis	2				Group II Partial bacteriostasis
3 hours complete bacteriostasis	5				
3 hours partial bacteriostasis	3				
	Total 10 cases (18%)				
3 and 4 hours	No inhibition				Group III No bacteriostasis
	Total 13 cases (equals 22%)				

60% of the cases showed complete bacteriostasis at four hours; 18% were partially bacteriostatic and 22% were not bacteriostatic after three and four hours. The cases in the partially bacteriostatic and non-bacteriostatic groups made equally satisfactory clinical progress as the infants in the completely bacteriostatic group. Of the thirteen non-bacteriostatic cases, eleven recovered completely from their infections and two died; one from bilateral otitis media and mastoiditis, due to *Staph. aureus* and complicated by nephritis and one from *B. coli* peritonitis following an extensive staphylococcal cellulitis.

The argument of the less efficient kidney applies to premature infants even more than to full-term ones. Penicillin was therefore given to five premature infants at six-hourly intervals. The serum of all of them was completely bacteriostatic six hours after injection of penicillin.

Methods of administration.—For systemic treatment the intermittent intramuscular route is the method of choice in infancy. It disturbs the infant but slightly if coinciding with feeding times, and the risk of secondary infection at the site of injection is negligible. The continuous intramuscular drip is not recommended in infants because of the likelihood of secondary infection at the site of the needle by excreta. Penicillin was given intravenously in our first cases, every four hours into the rubber tubing near the needle, but an increased tendency to thrombosis of the limb was noted. This route was therefore abandoned since maintenance of hydration of infants on penicillin is most important. Many infants tend to pass large quantities of urine whilst on penicillin treatment, an observation which has been made repeatedly. They do not gain weight during the course of treatment and their state of hydration has to be watched very carefully.

Local application of penicillin was given in addition when indicated.

(1) In three cases of septic arthritis penicillin was given intra-articularly as well as intramuscularly. Generally one systemic dose every twenty-four to forty-eight hours and sterilization of the joint cavity was achieved after seven days in all cases. No detectable amount of penicillin was present in the joint after forty-eight hours.

(2) In one case of meningitis, due to relatively penicillin-resistant hæmolytic streptococcus, penicillin was given intrathecally to supplement extensive systemic penicillin and sulphonamide treatment. One systemic dose of 4,000 units was injected every twenty-four to forty-eight hours and 1 to 2 units of penicillin were present after twenty-four hours, but no detectable amount after forty-eight hours.

(3) Penicillin was given into the diseased bone cavity in three cases of osteomyelitis every day to start with, and then every two to three days, combined with systemic treatment. Aspirations were sterile after one to two weeks in all the cases.

(4) Penicillin was injected into the pleural cavity in one case of empyema.

(5) In several cases of staphylococcal conjunctivitis, penicillin was applied locally in a solution containing 500 units per c.c. with very great success.

(6) Penicillin was applied to the skin as a cream containing 100 to 250 units per grammes. A variety of cases of pyoderma were treated. Better results were obtained when local treatment was combined with systemic treatment.

Selection of cases.—It is important to select cases for penicillin treatment carefully by clinical and bacteriological means. Every infant had a number of routine investigations carried out such as: rectal swab, post-nasal swab, swabs taken from all sites of obvious

infection, and a blood culture taken by the internal jugular vein technique. Cultures were made on suitable media and at the same time penicillin-sensitivity tests carried out by the agar cup method.

If the infant was thought to be likely to benefit from penicillin, treatment was commenced immediately after all necessary investigations had been initiated. Then after one to two days, the position was reviewed in the light of bacteriological results and treatment carried on or discontinued as indicated. This meant some wastage of the drug, but it has paid a good dividend in the long run to start treatment before major damage had been done. This lesson was learnt from the sad experiences at the beginning of the series when penicillin was in very short supply and sulphonamides were given prolonged and often unsuccessful trials before resorting to penicillin.

Complications.—A period of plenty of penicillin is fast approaching and a warning against its unrestricted use in infants may not be untimely. Although penicillin has not given rise to any toxic reactions in our hands, it has in not less than 18 cases out of 54, that is in one-third of the cases, paved the way for secondary infections, by Gram-negative penicillin-insensitive bacilli.

This does not include cases where Gram-negative bacilli were found in the course of penicillin treatment by bacteriological means only, but did not lead to any actual clinical disease.

B. coli was found ten times, *Bact. friedländer* five times, *Pseudomonas pyocyanea* four times and *Proteus vulgaris* once. Urinary infections, middle-ear and mastoid infections, bronchopneumonia, bacteraemia and peritonitis were caused by these organisms. These infections have at least contributed to death in six cases. There is some evidence that these Gram-negative bacilli are normally inhibited by staphylococci, streptococci, &c., and that they become uninhibited by the death of penicillin-sensitive organisms.

For the purpose of evaluating penicillin we have tried to keep clean penicillin cases and added sulphonamides only on evidence of secondary infection by penicillin-insensitive organisms. In view of the very real danger of secondary infection in infants, we feel justified in recommending combined penicillin-sulphonamide treatment from the very start. On the occurrence of a secondary infection penicillin should not be discontinued unless one can be reasonably certain that the primary infection has been dealt with successfully. In two cases of our early series we have discontinued penicillin after a short course on the discovery of a secondary infection, and at post-mortem we were faced with evidence of continued, severe, primary infection.

Analysis of cases.—A variety of conditions are included in a series of 62 cases, 57 of which were infants under the age of 1 year.

TABLE II.—ANALYSIS OF CONDITIONS TREATED. TOTAL OF 62 CASES, 57 OF WHICH WERE INFANTS

(1) Bacteraemia	21 cases	All infants
(2) Septic arthritis	3 cases	All infants (2 included under (1))
(3) Osteomyelitis	10 cases	7 infants (1 included under (1))
(4) Neonatal sepsis	3 cases without bacteraemia	
(5) Lung infections	9 cases	7 infants (4 included under (1))
(6) Congenital syphilis	4 cases	All infants
(7) Severe cellulitis	3 cases	All infants. No bacteraemia
(8) Tetanus	2 cases	1 infant
(9) Diarrhoea & vomiting	21 cases	(6 included under (1))
(10) Meningitis	1 case	1 infant
(11) Skin sepsis	} A number of cases	
(12) Eye sepsis		

(1) **Bacteraemia.**—In 14 of the 21 cases in this group coagulase-positive *Staphylococcus aureus* was isolated from the blood-stream, in 3 cases beta haemolytic streptococcus, Lancefield Group A, in 1 case both *Staphylococcus aureus* coagulase-positive and beta haemolytic streptococcus, Lancefield Group A, in 1 case pneumococcus and in 2 cases coagulase-negative *staphylococcus albus*.

The ages of the infants in this disease group varied from 4 days to 11½ months. Two had septic arthritis, one osteomyelitis, others presented with otitis media, mastoiditis, sepsis of the eye, umbilical sepsis, lung infection, pyoderma, nasopharyngitis and six presented as diarrhoea and vomiting.

Fifteen of these cases or 71% made a complete recovery. Of the 6 infants who died I had penicillin for less than forty-eight hours, 2 for four days only; this was early in our series and prolonged and extensive sulphonamide treatment had been tried unsuccessfully, and the use of penicillin thus delayed. In the 3 remaining infants the blood-stream was cleared of penicillin-sensitive organisms, but in 1 case *pseudomonas pyocyanea* was isolated from it. At post-mortem an abscess cavity in the heart muscle and bronchopneumonia with lung abscesses were found. *Pseudomonas pyocyanea* was grown from all these lesions.

Baby J. M.—Under penicillin treatment the clinical condition improved steadily, the rash disappeared, the rhinitis cleared, the liver and spleen decreased in size and the W.R. titre fell gradually. Ten weeks after the beginning of treatment, the W.R. was negative, the Kahn 1 plus positive. The X-ray changes of the bones had cleared up. After seven months the child is clinically normal, its W.R. and Kahn are negative.

DISCUSSION AND SUMMARY

Two hundred penicillin-level estimations in serum of infants were analysed and a dosage scheme suggested—1,000 units per pound expected body-weight in twenty-four hours, divided into four-hourly intramuscular doses. The incidence of Gram-negative bacillary, secondary infections is discussed.

The importance of adequate bacteriological investigations is stressed and combined penicillin and sulphonamide treatment is suggested pending the results of bacteriological investigations. An analysis of the cases treated emphasizes the prevalence of staphylococcus in serious neonatal infections, and the importance of penicillin treatment in those cases. Good results were obtained in cases of septicaemia and bone and joint sepsis.

A dosage scheme is suggested for congenital syphilis. Early results were encouraging, but follow up for many years will of course be necessary before the value of penicillin can be finally assessed.

A rather mixed group of cases of diarrhoea and vomiting was treated for relatively short periods. Under these conditions, results were not encouraging.

This work was carried out with Drs. W. W. Payne and P. Brand. I acknowledge gratefully the co-operation of the Honorary Medical and Surgical Staff and also the Nursing staff of the Hospital for Sick Children, Great Ormond Street. C. A. Cole, A.I.M.T., gave me valuable technical assistance. Miss Nora Hair kindly helped me in compiling the paper.

REFERENCE

- 1 GARROD, L. P., and HEATLEY, N. G. (1945) "Bacteriological Methods in Connection with Penicillin Treatment," *Brit. J. Surg.*, 32. Special Penicillin Issue.

[May 26, 1945]

MEETING HELD AT ST. HELIER HOSPITAL, CARSHALTON

CASES shown by Dr. J. N. O'REILLY

- (1) Diaphragmatic Hernia (X-rays only).
- (2) Diaphragmatic Hernia (Eventration) with Lipodystrophy.
- (3) Diaphragmatic Hernia Simulating Intrathoracic Tumour.
- (4) Diaphragmatic Hernia with Multiple Deformities
- (5) Cerebral Tumour—Surgical Removal (Dr. M. P. POTT for Dr. J. N. O'REILLY).
- (6) Oesophageal Stenosis
- (7) Congenital and Familial Ptosis.
- (8) Steatorrhoea with Anæmia.
- (9) Lipodystrophia Progressiva.
- (10) Polycystic Disease with Leukæmia.
- (11) Foreign Body in Duodenum.
- (12) Hemihypertrophy.
- (13) *Br. abortus* Meningitis (Dr. POTT for Dr. O'REILLY)

Section of Physical Medicine

President—L. DANYERS BAILEY, C.B.

[March 14, 1945]

Physical Methods in the Management of Septic Conditions

(Résumé of Introductory Remarks to a Clinical Meeting held at St. Thomas's Hospital)

Mr. J. M. Pullan: The damage caused by septic processes and consequent disabilities can be reduced by the rational use of physical methods as adjuncts to appropriate surgery. The more mechanically complex the structures involved in inflammation, the greater the danger of poor end-results. This is particularly well illustrated in the case of the hand. Whereas absolute rest appears to assist defensive reaction and to minimize the risks of spread of infection, it rapidly conduces to stiffness. It is, therefore, essential to strike a balance between complete rest and repeated mobilization of structures concerned in movement.

Constant vigilance is of the highest importance, not only to detect early signs of complications and to take steps to avoid them, but also because, in a very few instances, physical methods appear to have been the cause of a flare-up.

Dr. P. Bauwens: If we regard the application of poultices, fomentations, &c., as forms of physical therapy, it can be said that physical therapy has for several centuries played a valuable part in the treatment of septic conditions.

It is probable that, in future, physical methods will increasingly be called upon to take their place by the side of surgical measures which they cannot replace. If so, it is one of the aspects of physical medicine which will demand team work involving the surgeon, the bacteriologist, and the specialist in physical medicine.

The physical management of septic cases is not limited to the mere prescription of one or two measures; it entails the outlining of a course of treatment which may require constant modification as the condition progresses.

From the point of view of physical treatment and also for the sake of convenience, a septic condition can be considered to pass through four arbitrary phases. (1) The acute stage; (2) resolution; (3) repair; (4) restoration of function (or rehabilitation). A latent stage preceding the acute stage might be added.

The routine treatment may be outlined as follows:

1st Stage (Acute).

(a) Rest, by extensive immobilization—e.g. Elastoplast to skin after suitable preparation. Plaster of Paris slab.

(b) Local pyrexia by means of low intensity U.H.F. (ultra high frequency).

(c) Movement—active if possible.

(d) Improvement of general condition by esophylactic doses of U.V.R. (ultraviolet radiation) (E, reaction, in sections).

2nd Stage (Resolution).

Slough, if any, separates. Acute symptoms regress. Danger of spread is decreased.

(a) Rest by immobilization, restricted to affected part and immediate vicinity.

(b) Local pyrexia.

(c) Movement—active if possible.

3rd Stage (Repair).

Slough and necrotic tissues have been expelled. Granulation starts.

(a) U.V.R. 4th degree doses to the raw areas once or twice a week, to bring about production of repair hormones (Nutini and Loofbourrow).

(b) Packing and dressing with cod-liver oil. (Oxidizing properties of C.L.O., due to unsaturated nature of oil.)

(c) Discard of rigid splinting, provided movement does not interfere with proliferation. Movement may be restricted by other less drastic methods.

(d) Active movements.

4th Stage (Restoration of Function).

In most cases the earlier part of this stage overlaps the latter part of the preceding stage.

but appropriate treatment is started as soon as permissible. The methods employed in the 3rd stage may therefore be continued.

(a) Heat in suitable form, if indicated, to increase local temperature and produce hyperæmia. (U.H.F., radiant heat, wax baths.)

(b) Exercises, occupational therapy, to promote movement.

The routine plan just outlined may be supplemented by other physical methods when indicated, and modified to suit the existing circumstances. For instance:

Œdema, which constitutes a great hindrance to repair processes and also to mobility, can be controlled by means of massage, elevation of the limb, faradism under pressure, firm bandaging. (Crepe bandages, elastic webbing, Elastoplast or semiplast.)

Adhesions—contracted scar tissue—keloid and persistent induration can be attenuated by means of iodine ionization in superficial conditions, or X-ray therapy when deeper structures are involved.

Circumscribed allergic skin reactions such as are occasionally encountered in the course of localized infections (erysipeloid) appear to respond to the electrical introduction of the adrenaline and calcium ion into the affected regions.

While on the subject of electrical introduction of ions, I should like to mention that, in collaboration with my surgical colleagues, we have for some time made use of what might be termed "electro-chemotherapy". As is vaguely implied, electricity is employed to drive ions possessing the property of inhibiting pathological organisms into affected tissues.

Of the sulphonamide group of drugs, sodium sulphathiazole and sulphacetamide are on trial and appear to be giving gratifying results.

More recently, we have used sodium penicillin. Both the technique and the posology are still the objects of experimentation, but I think this method of treatment may prove of value in conjunction with surgery when it steps out of the experimental phases.

At all times the patients remain under the surgeons-in-charge. To them I am indebted both for entrusting me with the physical treatment of their cases and for allowing me to demonstrate the methods used. I am particularly grateful to Mr. R. H. Boggon who is in charge of the segregated septic cases in this hospital.

[April 14, 1945]

The Physical Basis of Radiant Heat Therapy

By DAVID S. EVANS and K. MENDELSSOHN¹

(From the Nuffield Department of Clinical Medicine, Oxford University)

IN clinical usage the term "radiant heat" usually refers to radiation in the red end of the visible spectrum ($0.65 \mu - 0.73 \mu$) together with the invisible infra-red rays ($0.73 \mu - 10 \mu$). As a physical phenomenon infra-red radiation is distinguished from X-rays, ultraviolet rays and visible light only by its greater wavelength. All these radiations are electromagnetic waves and represent a flow of energy emanating from the radiation source. The intensity of such radiation is determined by the quantity of heat developed in a body (known as a black body) which absorbs all the radiation falling on it.

However, although these various types of radiation can all be put into the same class of physical phenomena, their physiological effects, and hence their clinical applications, are widely different. For example, a physiological reaction, such as the production of vitamin D, which can be brought about by irradiation with feeble ultraviolet radiation cannot be effected at all by infra-red rays, even with intensities a thousand times as great. Many similar examples, illustrating the great variety of effects which are produced by different kinds of radiation, could be given, but they can all be reduced to a fairly simple scheme by considering the physical nature of the phenomena.

The difference in action between short- and long-wave radiation can readily be understood by reference to the quantum theory, which states that radiant energy is not to be regarded as a continuous stream, but is made up of "atoms" (quanta) of radiation, each of energy $\epsilon = h\nu$ where h is a constant (6.6×10^{-27} erg seconds) and ν is the frequency of the radiation ($\nu = \frac{c}{\lambda}$).

¹Working with a personal grant from the Medical Research Council.

This shows that quanta are not all of the same energy, but those of shorter wavelength (higher frequency) are bigger than those in long-wave radiation. Since the constant h is of very small size, the discontinuous nature of radiation is not apparent to our gross senses, but this property becomes of primary importance when the effect of radiation on atoms and molecules, including those of living tissues, has to be considered. In general, radiant energy is taken up by agglomerations of molecules in the form of an increased vibration of these molecules; that is to say, there is an increase in their temperature. However, if quanta of sufficient energy, depending on the particular species of molecule, are supplied, they may be able to effect a structural change in the molecule itself, that is, the radiation will produce a chemical change. It now becomes clear why a few quanta of ultraviolet radiation (whose energy is large since the radiation is of short wavelength) can produce an effect which can never be produced by even an enormous number of the smaller infra-red quanta, the reason being that the latter contains no single quantum big enough to effect this particular chemical change in the molecule.

It is true that the greater part of the energy of ultraviolet radiation, or the still shorter X-rays, goes into producing a rise of temperature when these rays are absorbed by the tissues, but the striking effects produced by the few quanta involved in chemical reactions overshadow this thermal effect. The particular property which distinguishes infra-red radiation on the other hand is that, when absorbed in the tissues, it produces no specific reaction and causes nothing but a rise in temperature.

This statement seems fairly safe, since the therapeutic effects, such as vasodilatation, increase in surface circulation, and desensitization of nerve ends, which are produced by infra-red, can be explained by the rise in temperature of the tissues. This distinction between specific and non-specific energy absorption by the tissues, which is explained by the quantum effects, makes it clear why we refer to infra-red radiation as "radiant heat"; the expression implies that we can with impunity supply so much energy to the patient that he registers the increased molecular vibration as heat sensation. No such course is possible with ultraviolet or X-rays because the attendant specific chemical reactions produce harmful effects at intensities far too low to cause a noticeable increase in temperature. It is significant that the total energy taken up by the patient in a single treatment with ultraviolet amounts to about 10 calories only, whereas as much as 25,000 calories may be administered in a single local treatment with infra-red and up to 200,000 calories in a single general treatment with an apparatus such as a radiant heat cradle. The lack of specific action of infra-red radiation, and the absence of insidious chemical changes such as are produced by even small doses of short-wave radiation, provide an ideal process for pumping energy into the patient. The same fact shows that we are unlikely to produce any therapeutic effects with infra-red except by energy doses much larger than those employed in X-ray and ultraviolet therapy. Large doses of infra-red will have to be administered with a certain amount of care and control, for, in general application, they may become comparable with the normal energy excretion of the whole body, and even in local application clinically effective doses of infra-red are likely to tax severely the capacity of the body for energy removal from the irradiated area.

Our first task must therefore be to determine the total energy flow received by the patient. The quality or "colour" of the radiation will have a certain effect, but, because of the non-specific nature of the effects of infra-red radiation, this factor will not be of the same crucial importance as it is in the case of short-wave radiations. The chief danger associated with the administration of infra-red radiation is that of giving an overdose sufficient to upset the processes of energy removal from the body. This means that an error of a few per cent. in the estimation of the applied radiant heat is not likely to lead to serious consequences, and a very high accuracy is therefore not required of an indicator for use in clinical practice. On the other hand, neglect of certain, not immediately obvious, physical factors, can, as we shall see, lead to the application of doses up to 200% larger than is intended, and we must therefore make a brief analysis of the physical factors involved.

First, we consider the sources from which the radiation comes. Any heated body emits radiation, and, if radiation reflected from its surface be neglected, the amount and wavelengths of the emitted radiation depend only on the absolute temperature of the body. The energy emitted from one square centimetre of the surface of a hot body (strictly a black body in the sense used above) in various wavelengths and for a series of temperatures is shown in fig 1. The curves for different temperatures all have a similar shape, but the wavelength in which the maximum energy is emitted becomes shorter the hotter the surface. The total energy emitted at each temperature is represented by the area under the appropriate curve, and, since the curves do not intersect,

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However, although these various types of radiation can all be put into the same class of physical phenomena, their physiological effects, and hence their clinical applications, are widely different. For example, a physiological reaction, such as the production of vitamin D, which can be brought about by irradiation with feeble ultraviolet radiation cannot be effected at all by infra-red rays, even with intensities a thousand times as great. Many similar examples, illustrating the great variety of effects which are produced by different kinds of radiation, could be given, but they can all be reduced to a fairly simple scheme by considering the physical nature of the phenomena.

The difference in action between short- and long-wave radiation can readily be understood by reference to the quantum theory, which states that radiant energy is not to be regarded as a continuous stream, but is made up of "atoms" (quanta) of radiation, each of energy $\epsilon = h\nu$ where h is a constant (6.6×10^{-27} erg seconds) and ν is the frequency of the radiation ($\nu = \frac{c}{\lambda}$).

¹Working with a personal grant from the Medical Research Council.

the flow of radiation, coming from all directions which would pass through a unit surface in the place of the patient's skin, and he should determine the amount of this energy received by direct measurement with a suitable instrument and not attempt to deduce it from such data as the power of his treatment lamp.

As a clinical unit suitable for specifying the energy received by the skin of a patient we have adopted the gram-calorie passing through a square centimetre in one minute. Since this definition, containing an energy, an area and a time, is somewhat cumbersome, we propose the short and simple name *pyron* for this unit.¹

As an example of the various physical factors which play a part in producing the total energy flow received by the patient we take an infra-red source in common use—the radiant heat cradle. This has been discussed in detail elsewhere (Evans and Mendelssohn, 1944) and we therefore confine ourselves to the main features. An element of the skin of a patient beneath the cradle receives radiation from three different types of source: (i) the filaments of the lamps; (ii) the glass envelopes of the bulbs; and (iii) the metal background of the cradle.

Sources (i) and (ii) radiate at full strength within about a minute of switching on the cradle, but source (iii) only reaches its power after more than an hour, when the metal background has reached equilibrium. Although it radiates from each square centimetre of its surface only about one-thousandth of the energy emitted by one square centimetre of lamp filament, the metal background is so extensive that it occupies a considerable part of the radiating hemisphere, and we must not, as has sometimes been done, neglect its contribution to the flux received by the patient. In fact, it has been shown, both by computation, and by direct measurement, that a square centimetre of skin in the centre of the cradle will receive about 0.5 pyron from sources (i) and (ii) and about 1 pyron (all in long-wave infra-red) from source (iii). In other words, a patient put under the cradle will receive three times as much radiation after an hour as he did at the beginning of the treatment. Thus, if the initial conditions under the cradle had been taken as those specifying the treatment, it is clear that, after some time, the patient (or a patient put under a similar cradle which had previously been warmed up) would have received an overdose of 200%. The therapist should, therefore, keep this time factor in mind, and should check the radiation flux administered to the patient in the course of treatment if there is a danger of parts of the treatment source warming up gradually.

The difficulty of estimating the actual amount of radiant energy administered is aggravated by the fact that some of the thermo-radiometers (instruments for measuring radiation flux) which have been proposed for clinical use will not register any of this large amount of long-wave radiation. In order to obtain quick response and a high degree of accuracy, glass-enclosed vacuum thermo-elements are sometimes used to measure radiation flux. Such an instrument will register accurately the flux received from the lamp filaments, but practically the whole long-wave flux coming from the comparatively cool cradle background (cf. fig. 1) is absorbed in the glass envelope and is left unregistered. Mayneord and Tulley (*loc. cit.*), who describe such an instrument for clinical use, stress this deficiency, and point out that the thermo-couples so far in use should be employed only in conjunction with a source emitting nothing but short-wave infra-red.

It is felt, however, that any instrument, the use of which is restricted to certain physical conditions the assessment of which may be difficult for the clinician, will be of rather limited practical use, and we have therefore tried to develop a thermo-radiometer which will register the total energy, independently of its wavelength. It is fortunate that the advantages of the vacuum thermo-couple—high sensitivity and very high accuracy, qualities most desirable in an instrument for physical investigation—are not essential in an efficient clinical indicator. Compared with the intensities registered in many physical researches, those employed in clinical work are enormous, and an error of even 10% in estimating the dose is likely to be well within the range of tolerance as between different patients. It is clear that a thermo-radiometer which registers infra-red radiation under all conditions of clinical treatment within a few per cent. of the true value will probably be of greater use to the therapist than an extremely accurate instrument, which, when wrongly employed, will indicate only a third of the dose actually administered (e.g. fig. 4).

A thermo-element does not in itself register an energy but a temperature, and only by determining by some primary physical method the radiation flux which will raise the receiver element to a given temperature can we calibrate such an instrument. If we dispense with a glass envelope the receiver temperature is affected, not only by the incident radiation, but also by the surrounding air. Its effects are produced in two ways: by heat conduction and by small air currents. The first effect can largely be eliminated

¹ This is in effect the same unit as that proposed by Mayneord and Tulley (1943), who, however, define it as "intensity of radiation" and state that it should be measured "perpendicular to the beam." Our definition merely extends the use of the unit proposed by these authors to include cases where no definite beam of radiation exists.

the total energy radiated from one square centimetre becomes greater as the temperature of the surface is increased. (The total energy radiated is proportional to the fourth power of the absolute temperature.)

If an incandescent source is to emit its maximum radiation in the ultraviolet it must be very hot—10,000 degrees absolute or more—and a relatively small source will emit a very large amount of energy. The cooler radiation sources, emitting energy chiefly in the infra-red, do not radiate much energy per square centimetre, and a source radiating mainly in the far infra-red (say 7 to 8 μ) must have a considerable area if it

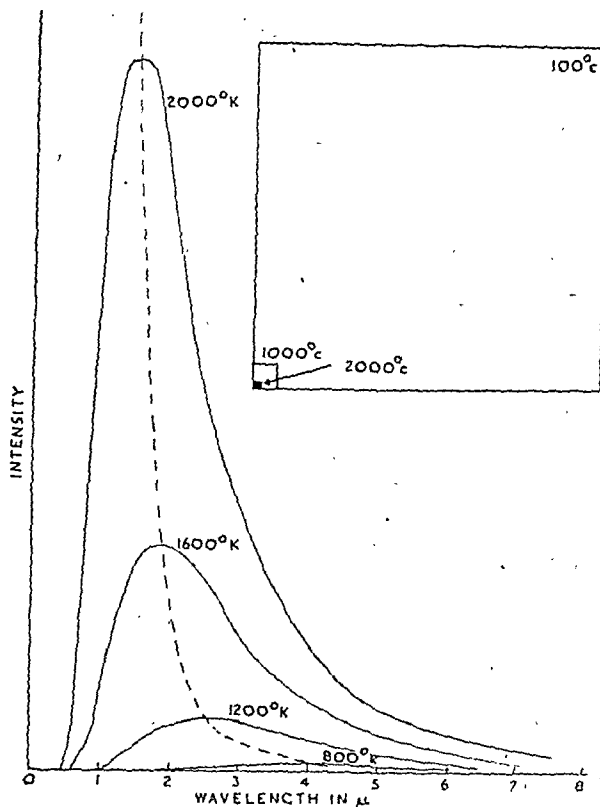


FIG. 1.—Relation between intensity and wavelength for radiation from (black) sources at different temperatures. The dotted line shows the wavelength of maximum intensity for different temperatures. The total energy radiated from a surface of given size at the temperature indicated is proportional to the area under the curve. Inset: The areas shown all give the same total emission of radiant energy to surroundings at room temperature.

is to emit an appreciable amount of energy. This is an important consideration for the therapist. A point source which would give a *beam* of radiation cannot be used since its output would be far too small, and extended radiation sources will have to be employed.

Even when there is no artificial source of radiation a patient is continually exposed to the radiation from his surroundings. For example, an undressed patient standing in a room at 20° C. receives from all directions the radiation appropriate to this temperature, but his skin, which is at, say, 30° C., will emit more radiation than it receives. Clearly what matters for clinical application is not the absolute amount of energy received, but the excess over that which the patient will normally receive from his surroundings: in addition, when considering the amount of radiation received by a portion of the patient's skin, we must take into account *all* the radiation emanating from within a hemisphere described about the skin element under consideration. If, as is often the case, this hemisphere contains bodies (e.g. lamps, hot metal shields, the walls of the room, &c.) at various temperatures and at various distances, the radiation from which arrives at various angles on the skin, all these factors must be taken into account. It is clear that an estimation of the actual clinical dose from a consideration of the effects of the various energy sources involved may in many cases be quite impossible owing to the mathematical difficulties involved. The quantity on which the clinician should base his treatment is

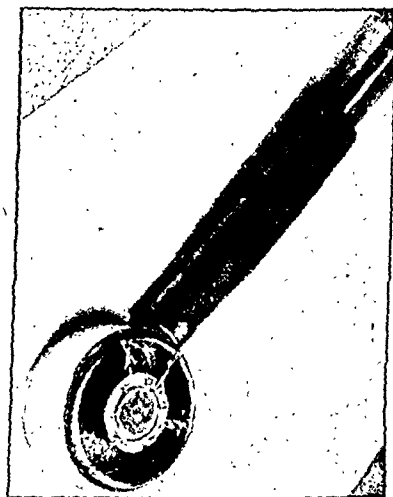


FIG. 2.—Thermo-radiometer. Photograph shows the receiver. The leads emerging from the handle are the electrical connections to the calibrated millivoltmeter and the tubes for the water cooling.

Nothing has been said so far about the reflection of radiation, either from parts of the source, or from the skin. The polished metal reflector of a treatment lamp will not necessarily reflect the rays from the source to the patient, and, in fact, will only do so if the reflector has a particular shape, e.g. that of a paraboloid with the radiation source at the focus. If favourable geometrical conditions are absent the amount of reflected radiation reaching the patient may be small. In our work on cradles we found that reflection played only an insignificant part in producing the flux received, because the positions of the lamps resulted in multiple reflections in which energy was dissipated in warming up the cradle background. These considerations are of importance to the designer of therapeutic radiation equipment, but need not worry the clinician, for, with his thermo-radiometer, he determines the radiation flux actually received by his patient irrespective of whether it has come direct from the source, has been reflected, or is secondary radiation from parts of the equipment warmed up by primary radiation from the source.

Reflection by the skin is usually considered to be about 20% of the total radiation incident upon it. This again is a point which need hardly disturb the clinician, for the reflected percentage will be roughly the same for all patients and for all parts of the body. If, therefore, treatment is based on determination of radiation doses with a thermo-radiometer, and on the clinically observed effects of these doses, it is a matter of indifference to the therapist whether or not a certain percentage of the radiation has been reflected. It is likely that there will be a variation of the reflection with wavelength employed (Oppel and Hardy, 1937), and this, as well as the more important question of the dependence of the absorption processes on wavelength (Bachem and Reed, 1931; Laurens and Foster, 1937), can only be settled by further research.

In some cases radiant heat is not applied directly to the skin, but through a blanket or other covering. In this case the estimation of the energy received by the patient is not so simple. A certain proportion, probably dependent on wavelength, of the original radiation will be transmitted through the interposed material. The radiation absorbed by the material will raise its temperature and cause it to act as a secondary radiator, and in addition, there will be a transfer of energy by conduction. The last two items will depend on the temperature acquired by the interposed material and this will depend very much on the conditions of treatment. If, for instance, the interposed material is free to lose heat by air currents, its temperature, other things being equal, will be much lower than in still air. The first item, the proportion of incident radiation transmitted, can be determined with some certainty and has been measured by us for a number of common materials. Radiation from an incandescent filament lamp (radiation maximum $\sim 1.5 \mu$) and from an open electric fire (radiation maximum $\sim 3 \mu$) with equal fluxes of about 1 pyron were used. Table I gives the percentages of incident radiation transmitted by the materials in the two cases.

TABLE I.—PERCENTAGE OF INCIDENT RADIATION FLUX TRANSMITTED THROUGH VARIOUS MATERIALS.

Material	Source	
	Lamp	Electric fire
Lint	30	22
Blanket	25	19
Cotton	48	30
Linen	44	30
Towel	27	23

TABLE II.

Total flux from fire	2.15 pyrons
Transmitted by lint	0.59 pyron
Re-radiation	0.02 pyron
Conduction	0.69 pyron
Total 1.30 pyrons	

It can be seen that a somewhat greater proportion is transmitted of the radiation from the source giving the shorter wavelength. The experiments were checked by a repetition using about double the radiation flux. The tabulated figures should not be taken as indicating more than the order of magnitude of the transmitted proportions.

The energy received by the patient by conduction and secondary radiation will vary greatly in different circumstances, and there is no simple way of assessing these contributions. We have determined them separately in one case. The thermo-radiometer was placed at a given distance from an open electric fire and the flux noted. A piece of lint was interposed close to the receiver, and the transmitted energy noted. The lint was left in position until it had warmed up so that the thermo-radiometer then indicated the transmitted energy *plus* the secondary radiation from the lint. The thermo-radiometer was then replaced by a calorimeter which registered the *total* energy received by transmission secondary radiation and conduction. The receiving surface of the calorimeter was in direct contact with the lint, probably simulating to some extent the condition of the skin of a patient covered with a layer of lint. The energy contributions are shown in Table II.

by placing the cold reference junction in close proximity to the recording junction. We have already described the principle of an instrument in which this has been done (Evans and Mendelssohn, 1944), its essential features being two receiver plates attached to two thermo-junctions, one plate being exposed to the radiation from the hemisphere to which the patient's skin is exposed, and the other to a hemisphere artificially kept at room temperature. Fluctuations due to small air currents can be overcome by increasing the area and thermal capacity of the receiving surface. We have to pay for this by the inability of the instrument to record instantaneously, but this is not of great importance in clinical use.

We have now perfected the laboratory type of instrument previously employed to a form suited to clinical use (fig. 2). It records the radiation flux applied in clinical therapy within a few per cent., and a final reading is obtained in about thirty seconds. The blackened background opposed to the second (reference) receiver plate can be watercooled if the instrument is to be used for continuous measurement under conditions (e.g. in a hot cradle) such that the thermal capacity of the background would not be sufficient to keep it down to room temperature, but watercooling is not essential if the instrument is to be used only for occasional determinations under a treatment lamp. Using the instrument we have determined the energy profiles of two common treatment sources (fig. 3, *a* and *b*).

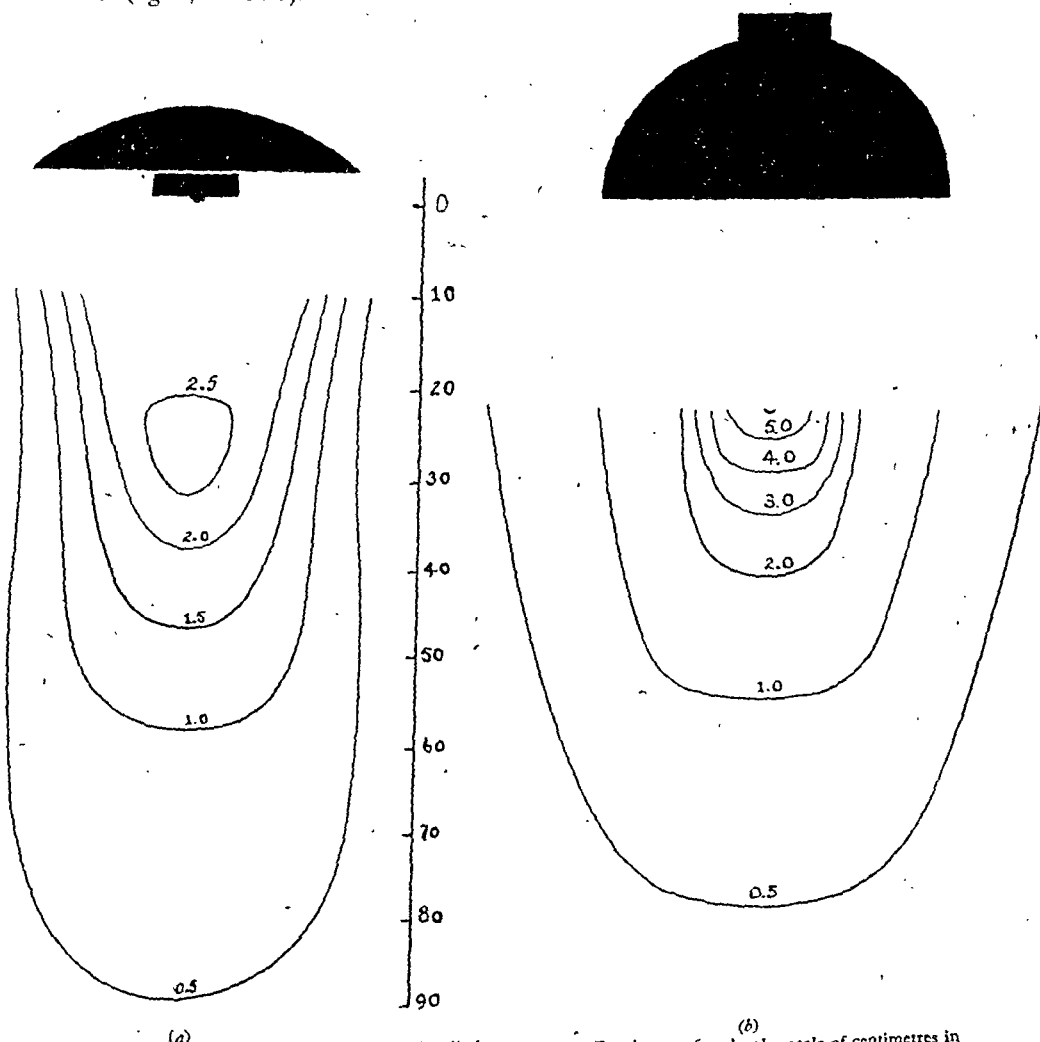


FIG. 3.—Energy profiles of two clinical radiation sources. Receiver surface level: scale of centimetres in centre. (a) Dull emitter source (Infra-red-ray generator of the General Radiological Company). (b) Bright emitter source (1,000 watt lamp, Universal Radiant Heat Apparatus, by Universal Domestic Products Ltd. As supplied to E.M.S.).

by an air space, the bare skin is likely to receive only a negligible amount of energy by conduction.

Taking the other extreme, when the bare skin of the patient is irradiated in a completely enclosed space (fig. 5) we can arrive at the result by the following consideration of the energy balance: the total energy output of the source has to be dissipated, and a certain fraction reaches the skin of the patient. The question is whether this fraction would be different if the space were evacuated, thus eliminating air conduction. If we make the apparently reasonable assumption that the losses to the outside are the same whether the space is evacuated or not, the same amount of energy should be received by the skin in both cases. When there is no air the radiation arrives direct and there is of course no conduction. When the space is filled with air, it absorbs a little of the radiation, but the warmed air then repays this by conduction. In this case also we can therefore neglect air conduction if we are concerned only with the total energy supplied and not with the mechanism which transmits it. Air conduction will, however, play an important part when the skin of the patient is covered by material such as a blanket, either in direct contact with it, or separated by a narrow air space. In such a case, air conduction adds its contribution to the energy transmitted by the covering, but in all cases the covering reduces the energy flow to the patient by the amount reflected from the upper surface of the covering back towards the original source.

Fig. 5 leads to another interesting consideration. Unless energy is continually removed from the irradiated tissues, these will take up a temperature similar to that of the rest of the enclosure. In the case of the cradle, the enclosing surfaces, blankets, metal background, &c., may become too hot to touch. This is not surprising considering the large amounts of energy used in radiant heat therapy. The fact that the skin temperature is only slightly raised under the same conditions is, of course, due to the physiological processes responsible for the removal of energy from the irradiated region, i.e. perspiration and blood circulation. The increase in vasodilatation under infra-red radiation which causes a more rapid removal of energy from the body surface is clearly a defence mechanism against overheating of the skin. A detailed survey of the processes of energy absorption would be a most complex matter, clearly falling outside the scope of this paper, but a few general conclusions may safely be drawn on physical grounds. First, infra-red therapy can never remain a purely local treatment since the energy pumped into any part of the body by radiation will be removed to other parts of the body, and the process of removal will even be speeded up by the application of the radiation. Secondly, there must be a threshold of radiation flux beyond which the removal processes will be unable to prevent local overheating, and when this is passed there will be a rapid rise in skin temperature, finally causing a radiation burn. This threshold is likely to depend on the wavelength employed, because it appears that short-wave radiation has a deeper penetration into the tissues than long-wave infra-red. Although a certain amount of work has been done on these problems information on the relation between heat sensation, local heat production, and depth of penetration under high radiation fluxes is too incomplete to allow definite conclusions to be drawn. In particular a well-founded determination of the limits of tolerance would be desirable. Here we meet immediately another difficulty. If irradiation just below the tolerance limit is carried out on a restricted skin area, we assume tacitly that the total energy received by this skin area will be lost by the rest of the body without difficulty. However, if we now increase the area irradiated, we must eventually reach a stage when the total energy received can no longer be lost without difficulty. This means, of course, that the tolerance limit must decrease as the area of irradiation is increased. For instance, the energy received under a heat cradle is about 200,000 calories per hour, or about twice the normal metabolic heat production. Normally, about 20,000 calories per hour are lost by evaporation (insensible perspiration), the remainder being lost by convection and radiation, but under the cradle, neither of these two latter modes of heat excretion is open to the patient, and he must dissipate his entire intake of heat, together with his own metabolic heat, by means of perspiration. This means that instead of losing about 40 grammes of water per hour by evaporation, he must now evaporate about 600 grammes per hour. Again, these figures only indicate the order of magnitude and neglect such changes as, for example, a decrease in the metabolic heat production. Even so, it is clear that these conditions must tax severely the heat removal processes of the body, and, indeed, irradiation under a cradle can be used as a means of raising the body temperature.

This brings us to the induction of pyrexia and hyperpyrexia by means of radiant heat, for, if we prevent heat loss by evaporation by saturating the air inside the cradle or heat bath with water vapour, the heat losses by respiration, and by perspiration from

This shows that about 60% of the original energy reaches the skin when a layer of lint is interposed, half of this being due to transmitted radiation, and half to conduction, secondary radiation in this case being very small. Obviously this last item might have been much larger if conditions were such as to allow the lint to reach a higher temperature, as might happen in a cradle or under a closed lamp.

Conduction processes, such as that described above, lie, strictly speaking, outside the domain of radiant heat estimation, but, as we have seen, the application of infra-red consists in nothing but the pumping of thermal energy into the patient, so that the therapist will be interested, not only in energy received by radiation, but in the total energy received in all ways, including conduction. This presents more difficulty than the measurement of radiant heat proper. The calorimeter used by us, which was specially developed for these investigations, is a laboratory instrument which has to be used with discretion, and the reduction of its readings entails some computation. Some simplification might be possible, but it is uncertain whether an instrument, giving a direct reading as the thermo-radiometer does, could be devised for general clinical use. On the other hand, general physical argument enables us to assess the amount of conduction in some important therapeutic conditions. Under a treatment lamp separated from the patient

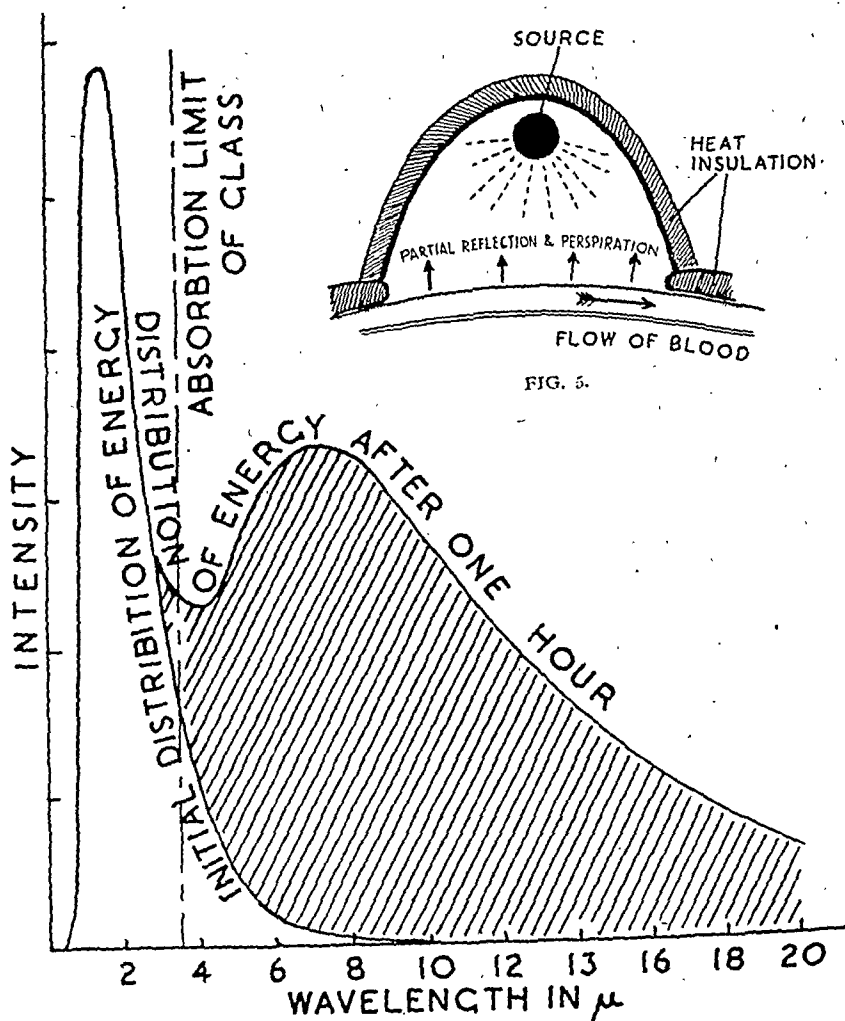


FIG. 4.

FIG. 4.—Radiation flux in cradle in various wavelengths immediately after switching on and after one hour, showing that the additional flux is all beyond the limit of transmission of glass, and will therefore, not be registered by glass-enclosed radiometers.

FIG. 5.—Conditions under an enclosed radiation source.

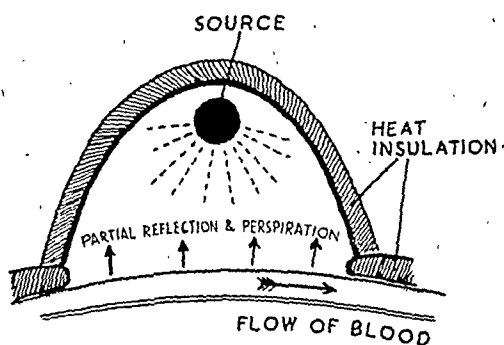


FIG. 5.

Section of Neurology

President—Air Vice-Marshal C. P. SYMONDS, C.B.

[December 14, 1944]

Orbital Tumours

By HARVEY JACKSON, F.R.C.S.

WHILST Dr. Walter Dandy's monograph on "Orbital Tumours" (1943) presents many valuable data there remain a number of equivocal points from both the clinical and the pathological aspects of the subject; some of these, it is hoped, are to be clarified in the present paper through the augmentation of the basic material. This additional material for review is provided by a paper under the authorship of Iles and Rendle Short (1943) together with personal cases. Altogether these three series afford a fairly representative cross-section of neoplastic lesions likely to be encountered within, or encroaching on, the orbit, though by no means pathologically exhaustive.

Personal interest in the subject was initiated in 1936 when Mr. Gibb and Dr. Grainger Stewart referred a female child, $4\frac{1}{2}$ years of age, who was suffering from a tumour of the optic nerve. A decision was invited as to the feasibility and advisability of excision of the growth with conservation of the eyeball both for æsthetic purposes and as a controlling influence in the maintenance of normal orbital development. Inquiry of ophthalmological colleagues as to the possible outcome of an eye so depleted of vascular and trophic supplies remained inconclusive. Admittedly Parsons (1942) states that "it is possible in some cases of optic nerve tumour to remove the growth while retaining the eye". Excision of the whole nerve from globe to chiasma was carried out; it contained a tumour some 2.5 cm. in length by 1.5 cm. in diameter (fig. 6). Fortunately the final result of our deliberations is the existence, at the present time, of a healthy girl of 13 years of age, with quite a presentable appearance, both eyes being freely mobile and the blending of these bears favourable expression. Since that time the problems of the diagnosis and treatment of orbital tumours have recurred with rather increasing frequency. Additional material for consideration of the surgery of the orbit has been provided in cases of advanced "exophthalmic ophthalmoplegia", a disease to be seriously debated in its differentiation from orbital tumour when the former is of unilateral distribution.

Incidence.—With what frequency orbital tumours occur is difficult to assess, but they are surely uncommon. True orbital tumours, in other words those limited to the orbital cavity, form a limited number of the three series under review. It may be that tumours lying in the anterior approaches to the orbit are more common, but they do not come to the notice of the neurosurgeon. It is most noticeable how many more women are involved than men.

Differential diagnosis.—The differential diagnosis of "orbital tumour" is so intimately related to that of "unilateral proptosis" that many points of discussion must be formulated along such lines. One of the simplest means of attacking the diagnosis would seem to evolve from a discussion of the several complaints that influence the patient to solicit surgical aid; it is in this manner that the writer proposes to proceed. Those lesions most likely to be confounded are: exophthalmic ophthalmoplegia, certain generalized bone diseases, meningocele or encephalocele, and vascular lesions of aneurysmal or of an arteriovenous fistulous nature.

Symptoms and signs.—The paramount complaint made by patients is that of unilateral proptosis wherein there is an irreducible progressive, axial, and non-pulsatile protrusion of one eye. This naturally arises out of the relative disproportion between the volume of the orbital contents and the capacity of the orbital cavity. In order that an expanding, space-consuming lesion be harboured one or more of the following processes must take effect: displacement of normal content, atrophy of normal content, or enlargement of the bony cavity. Each of these, no doubt, plays a part in accommodating the new structure. In consequence of the several possible compensating factors it becomes apparent that the degree of each depends on the amount of the other two—in this way one can best explain the not unusual lack of proptosis in some cases of glioma of the optic chiasma on their invading the orbit. Dandy (1943) draws particular attention to this possibility of orbital invasion without proptosis. However, a chiasmal glioma even with orbital extension is not a tumour

the head will be quite inadequate to counterbalance the heat intake, and the body temperature will rise rapidly. The clinical observations on the efficiency and suitability of radiant heat for the induction of artificial hyperpyrexia are still somewhat contradictory (cf. Krusen, 1941) and it appears that a good deal of information concerning tolerance limits, maximum safe skin temperatures, and other relevant factors is needed before anything definite can be said about this type of treatment.

It seems to us that one of the main difficulties confronting the clinician who uses large doses of radiant heat will be to distinguish between local and general effects. This can be exemplified by the observation that in local application of heat, skin temperatures between 40° C. and 45° C. will produce no ill-effects (Mendelssohn and Rossiter, 1944) but it would be impossible to keep a patient for any length of time in a saturated atmosphere of this temperature.

SUMMARY

Infra-red radiation has no specific action on the tissues: its therapeutic value is due to the fact that it supplies them with energy in the form of heat. The determination of the total radiation flux reaching the patient should, therefore, be the first consideration.

An analysis of the physical factors involved shows that infra-red sources, particularly those emitting long-wave radiation, have to be of considerable area, which, in many cases, makes the technique of beam therapy inapplicable. This, together with the problem presented by secondary radiation, makes computation of dosage difficult, and treatment should, therefore, be based on the measurement of radiation flux incident on the patient's skin. A suitable instrument for clinical use has been described.

The effect of interposing various materials in reducing the incident radiation has been investigated, and it has been found that shorter wavelengths have, in general, a slightly higher penetrating power.

The effect of heat conduction through the air, incidental to radiant heat treatment, on the total heat supplied to the patient, has been discussed, and determined in one particular case.

A rough survey of the physical factors governing heat removal from the tissues shows that treatment by infra-red can never remain purely local.

ACKNOWLEDGMENTS

We are indebted to Professor L. J. Witts for his constant interest in this work, and to Dr. Violet Cyriax of the Department of Physical Medicine, Radcliffe Infirmary, Oxford, for providing facilities for the measurements on clinical radiation sources.

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that one may consider as being "orbital". One may rightly ask what degree of protrusion is necessary before a true orbital tumour is to be suspected? I submit that there is no correct reply to this question, but I would mention that in carrying out prolonged investigations on cases of proptosis of varied origins, Rundle and Wilson (1944) found that of all their cases of proven primary orbital tumours the minimal difference between the measurements of the two eyes was 6.0 mm. The protrusion of the most proptosed eye I have seen so far was of such a dimension that the eyelids occasionally became retained behind the globe, a state comparable with a paraphimosis. These more advanced degrees of protrusion in the writer's experience have resulted from juxta-orbital meningiomata and arteriovenous fistulae. The absence of, or failure to observe, signs other than proptosis generally leads to a diagnosis of "exophthalmic ophthalmoplegia"; indeed of my series, these cases which had not formed a palpable orbital or associated mass and did not show papilloedema had all, at one time or another, been so designated.

Just as the lack of proptosis does not of necessity prove that the orbit is uninvolved, so the presence of proptosis does not require orbital invasion by tumour. Actually unilateral and also bilateral proptosis are to be seen in correlation with intracranial tumours distantly placed from the orbit. The literature provides records of proptosis in association with subdural haematoma, basal tumours of the anterior and middle fossae, tumours of the cerebello-pontile angle, ventricular tumours and occipital tumours. Jacques Ley (1936) states that when unilateral proptosis accompanies cerebello-pontile angle tumours the proptosis is more common on the side opposite to the brain lesion. The incidence of proptosis with cerebral tumours in general bears different citation at the hands of different writers: while Skydsgaard (1938) gives the figure as 4%, Cushing and Gibbs (1922) say 8%, and Elsberg, Larr. and Dyke (1932) describe unilateral protrusion on 1.5 to 2.0% of cerebral tumours. In explanation Cushing and Gibbs offer the following theories: (i) Inverted Horner's syndrome; (ii) Oculomotor paresis; (iii) Hormonal—anterior pituitary; (iv) Compression of cavernous sinus.

When an intracranial lesion of very slow development encroaches upon, but does not extend into the orbit, a further process may be applied in explanation of the accompanying protrusion of the eye. The best example of the process that comes to mind is found in reaction to cysts of the jaw, wherein absorption of the bone adjacent to the lesion takes place and coincident deposition of bone occurs on the surface. This process in my opinion explained the clinical appearances in a young fellow afflicted by an intracranial epidermoid of the middle fossa, involving the pharynx and nasopharynx. In deciding on operative intervention, in this case, one was conscious of the undue risk of supervening meningitis, if not of chemical origin then from infection by organisms inhabiting the nasopharynx. This foreseen but none the less disappointing misfortune complicated the post-operative period with the result that the patient died. Autopsy proved that no direct extension of tumour affected the orbit but the bone between the middle fossa and the orbit had assumed that state of egg-shell crackling so often found in jaws containing dental or dentigerous cysts.

A proportion of the patients describe variability in the extent of the protrusion, as a result of various factors, i.e. change of posture, coughing, straining and sneezing, &c. This is based probably on vascular changes either within the orbit or actually in the tumour, and can be demonstrated clinically by jugular compression. A meningocele or encephalocele, of course, would show variability in similar fashion, but brought about in a different way—by increasing the intracranial pressure. Women patients not infrequently mention that changes are to be seen at, or about, the time of the menstrual cycle: what factor there is behind this is not certain; it may well be the same vascular project already mentioned, but it may equally well be of endocrinal origin. Infective granuloma—the so-called "pseudo-tumour of the orbit"—shows a variability together with which other symptoms such as pain also vary, and it would appear more likely that the change depended upon an exacerbation of the infective process, thereby producing more oedema and greater cellular infiltration, as well as some increase in vascularity. It seems possible that tumours arising in the region of the lacrimal gland may institute variability in yet another way, that is by interfering with the free escape of secretion. Lindsay Rea (1941) states that the proptosis associated with haemangiomas is influenced by posture, crying or other emotional disturbances.

On occasion one meets a patient in whom proptosis is marked and is said to have been almost of spontaneous development. One of my cases provided this history; he had a chromophobe adenoma of the pituitary which had invaded the orbit (fig. 4). The



FIG. 1A.



FIG. 1B.

FIG. 1A.—Patient of 46 years, who noticed the proptosis accidentally when trying on hats at a milliner's.

FIG. 1B.—Section of tumour removed at operation. A typical hamangioblastoma.



FIG. 2A. — Case with a temporal boss, edema of the eyelids, and a discharging sinus towards the outer canthus.

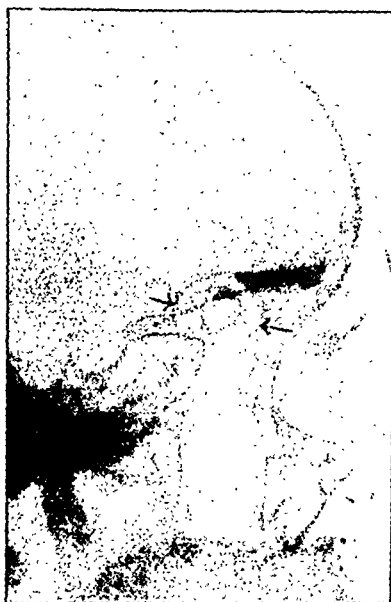


FIG. 2B.—Radiograph showing an erosion described by Dr. Dandy as typifying a case of "Schüller-Christian disease".



FIG. 2C.—Section shows the dermoid nature of the tumour.

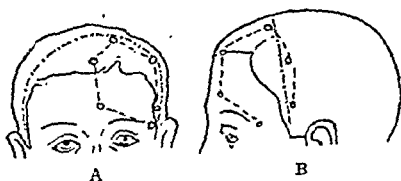
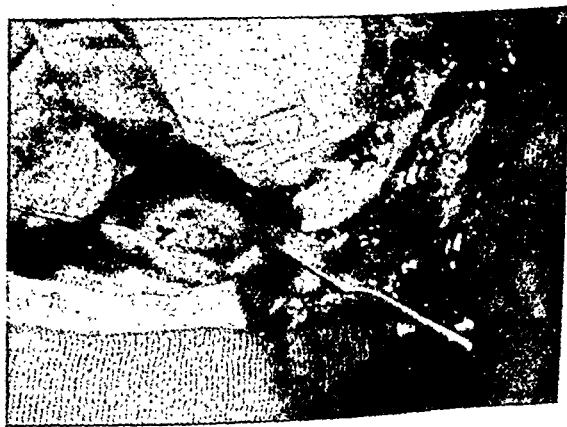


FIG. 3.—Sketches show plan of skin incision and osteoplastic frontal flap. Photograph shows the resultant exposure with a tumour about to be delivered.



C

that one may consider as being "orbital". One may rightly ask what degree of protrusion is necessary before a true orbital tumour is to be suspected? I submit that there is no correct reply to this question, but I would mention that in carrying out prolonged investigations on cases of proptosis of varied origins, Rundle and Wilson (1944) found that of all their cases of proven primary orbital tumours the minimal difference between the measurements of the two eyes was 6.0 mm. The protrusion of the most proptosed eye I have seen so far was of such a dimension that the eyelids occasionally became retained behind the globe, a state comparable with a paraphimosis. These more advanced degrees of protrusion in the writer's experience have resulted from juxta-orbital meningiomata and arteriovenous fistulae. The absence of, or failure to observe, signs other than proptosis generally leads to a diagnosis of "exophthalmic ophthalmoplegia"; indeed of my series, those cases which had not formed a palpable orbital or associated mass and did not show papilloedema had all, at one time or another, been so designated.

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protrusion was described as having appeared overnight. The impression was that an acute hæmorrhage into the tumour had occurred. Byers (1901) refers to sudden increase in exophthalmos and explains this as due to effusion into Tenon's capsule and the supravaginal lymph space of the optic nerve.

Visual deterioration.—Coincident with, at times even preceding proptosis, frequently there occurs visual deterioration in one or other of its forms: increasing hypermetropia, diplopia, restriction of the visual field, or diminution of visual acuity. Over a considerable time many tumours exert little influence on vision, but failure to appreciate a change owing to casual examination is responsible for misjudgment in some cases. Only by meticulous charting of the visual fields, applying small objects of 1 or 2 mm., and employing a Bjerrum screen are some of the lesser defects to be revealed. The recognition of such a defect can make all the difference in establishing a diagnosis, or in revealing intracranial involvement.

Strange though it may seem often both visual deterioration and ocular protrusion escape the attention of the patient; as a matter of fact the discovery of either can be purely accidental. A patient will only come to realize the paucity of vision because, for some reason or other, the good eye is temporarily put out of action, involuntarily, as when some foreign body enters the conjunctival sac, or voluntarily as in a patient who closed one eye in an attempt to sight a rifle. This unrevealed loss of vision no doubt accounts for the somewhat infrequent complaint of double vision from patients with these disorders. In like fashion the proptosis is ignored by the patient who, in retrospect, finds that it is of long standing—a woman patient first noted proptosis when trying on hats at the milliner's, yet the prominence of the eye exists in a passport photograph taken four years prior to this incident (fig. 1, A and B).

Diplopia, according to Parsons (1942), is a common complaint in optic nerve tumours. Whether this is so, or not, I cannot say, but of my limited number of these cases not one patient recorded it. The general impression of all cases of primary orbital tumours seen by the writer is that diplopia is not commonly found but was observed in approximately one patient in four. Already the attendant visual failure has been proffered as an explanation in some cases; in others it would seem reasonable to suppose a central suppression of the conflicting image.

Preceding visual deterioration, in what one may term the more absolute forms discussed hitherto, it is possible for relative inefficiency to develop as an increasing hypermetropia. This is brought about by direct pressure on the back of the globe, so compressing it in its anteroposterior axis. It is an unusual finding, having been noted in only one of my series. This, perhaps, is diagnostic of a tumour limited to the orbit.

The eye may be displaced in other directions than directly forwards, particularly by tumours lying at the orbital outlet. As far as I know there is nothing characteristic in such displacement.

Pain.—Generally speaking the outstanding point about pain is the lack of it. Of my patients in only two did pain pervade the picture; both cases harboured inflammatory masses—"orbital pseudo-tumours". So important did it appear in these cases that I am rather of the opinion that it may be a diagnostic feature.

Some reservation is necessary here, for another patient came to me because of pain in the distribution of the second division of the trigeminal nerve, with the diagnosis of "trigeminal neuralgia". He, at a later date, developed proptosis with full realization of the underlying disease—carcinoma of the maxilla. I may say that the original radiographs failed to indicate any difference between the two maxillæ. A similar case is presented in Dr. Dandy's series.

Tumour formation.—Apart from the formation of a mass superficially placed in the orbital outlet, it is unusual for any localized orbital swelling to attract the attention of the victim. More likely is it that a patient will be directed to the surgeon on account of increasing protrusion in the frontal or temporal region due to an underlying meningioma, or other pathological entity. Two patients of my series had had biopsies carried out on such temporal protrusions prior to my seeing them; one of these became infected in consequence, in fact it was the severity of the infection that led to his transfer. Occasionally one is able to feel the anterior margin of a mass tracking over the surface of the eyeball.

Alternative symptoms.—In addition to the above and more common complaints, various other symptoms have been responsible for the appearance of patients: amongst these symptoms may be mentioned ptosis, œdema of the eyelids, chemosis, cranial nerve palsies, an audible bruit, or a discharging sinus. While these symptoms obtrude as direct indicators of orbital involvement, tumours involving the orbit secondarily show in addition the associated clinical signs of their primary origin.

Retraction of the upper lid due to spasm of the levator palpebrae superioris is a rare finding in a case of orbital tumour. Rather is this considered to be an important factor in the differentiation of exophthalmic ophthalmoplegia, wherein this retraction is thought perhaps to be typical. I have a patient with this sign at the present time, in whom there is no doubt of the existence of a tumour, as it is palpable.

Dr. Dandy stresses the high proportion of cases in which, in his experience, both the orbit and the cranial cavity are involved—in his experience 75 to 80%. He also makes the following comment: "As a matter of fact, it is rarely possible before operation to be certain whether or not the tumour also lies within the cranial chamber, as so many of them do." The writer cannot subscribe to this statement. In fact my experience is that, by careful clinical examination, by judicious radiography, and by suitable application of laboratory investigation, not only is the diagnosis of tumour to be reached, but its ramifications regularly revealed, and not infrequently its pathological nature surmised.

Ophthalmoscopic examination.—The ophthalmoscope affords evidence of the escape or implication of the visual pathways in so far as the appearances of the optic disc apply. An occasional detachment of the retina is to be found. Parsons (1942) makes



FIG. 4.—A "spontaneous" proptosis said to have developed overnight. Case of chromophobe adenoma of the pituitary invading the orbit.



FIG. 5.—Section of an "inflammatory mass" or "orbital pseudo-tumour".

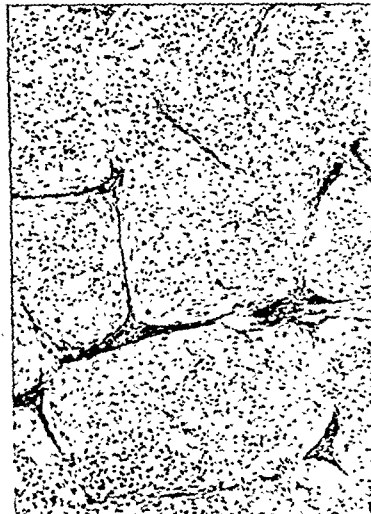


FIG. 6.—Section of "glioma of the optic nerve".

the concise statement that "papillitis may be present especially with optic nerve tumours, optic atrophy is common in other forms". As a generalization this statement holds, but some qualification seems to be indicated. Although primary atrophy would appear to be the final outcome of true orbital tumours, other than those of the optic nerve, no matter the plane of origin, the disc changes brought about in the juxta-orbital tumours are those peculiar to the primary lesion. Thus while primary atrophy is associated with a meningioma developing from the sphenoidal ridge or the olfactory groove, a temporal glioma is prone to produce papilloedema or its derivative, consecutive atrophy. Optic nerve tumours often give rise to gross papilloedema, and sometimes invade the disc.

Duration of the disease.—Naturally the rate of growth will vary with the pathological nature of the tumour. Nevertheless it is no uncommon story to find that an innocent tumour of the orbit has been known to have been present for anything up to twenty years. The cases of longest standing, in my experience, are the "epidermoids". Only by retrospective inquiry may it be possible to gain any idea of the duration, owing to the fact that the patient's attention has not been focused on the existence of an abnormality. However, experiences vary; in respect of my limited number of optic nerve tumours, the history has been of somewhat rapid deterioration lasting a few weeks to three or four months: yet Lindsay Rea (1941) says that these tumours grow slowly, citing periods of up to two years. Attention to intermittence or remittance in the clinical history has already been given, this would appear to be especially noticeable in orbital pseudo-tumour.

protrusion was described as having appeared overnight. The impression was that an acute hæmorrhage into the tumour had occurred. Byers (1901) refers to sudden increase in exophthalmos and explains this as due to effusion into Tenon's capsule and the supravaginal lymph space of the optic nerve.

Visual deterioration.—Coincident with, at times even preceding proptosis, frequently there occurs visual deterioration in one or other of its forms: increasing hypermetropia, diplopia, restriction of the visual field, or diminution of visual acuity. Over a considerable time many tumours exert little influence on vision, but failure to appreciate a change owing to casual examination is responsible for misjudgment in some cases. Only by meticulous charting of the visual fields, applying small objects of 1 or 2 mm., and employing a Bjerrum screen are some of the lesser defects to be revealed. The recognition of such a defect can make all the difference in establishing a diagnosis, or in revealing intracranial involvement.

Strange though it may seem often both visual deterioration and ocular protrusion escape the attention of the patient; as a matter of fact the discovery of either can be purely accidental. A patient will only come to realize the paucity of vision because, for some reason or other, the good eye is temporarily put out of action, involuntarily, as when some foreign body enters the conjunctival sac, or voluntarily as in a patient who closed one eye in an attempt to sight a rifle. This unrevealed loss of vision no doubt accounts for the somewhat infrequent complaint of double vision from patients with these disorders. In like fashion the proptosis is ignored by the patient who, in retrospect, finds that it is of long standing—a woman patient first noted proptosis when trying on hats at the milliner's, yet the prominence of the eye exists in a passport photograph taken four years prior to this incident (fig. 1, A and B).

Diplopia, according to Parsons (1942), is a common complaint in optic nerve tumours. Whether this is so, or not, I cannot say, but of my limited number of these cases not one patient recorded it. The general impression of all cases of primary orbital tumours seen by the writer is that diplopia is not commonly found but was observed in approximately one patient in four. Already the attendant visual failure has been proffered as an explanation in some cases; in others it would seem reasonable to suppose a central suppression of the conflicting image.

Preceding visual deterioration, in what one may term the more absolute forms discussed hitherto, it is possible for relative inefficiency to develop as an increasing hypermetropia. This is brought about by direct pressure on the back of the globe, so compressing it in its anteroposterior axis. It is an unusual finding, having been noted in only one of my series. This, perhaps, is diagnostic of a tumour limited to the orbit.

The eye may be displaced in other directions than directly forwards, particularly by tumours lying at the orbital outlet. As far as I know there is nothing characteristic in such displacement.

Pain.—Generally speaking the outstanding point about pain is the lack of it. Of my patients in only two did pain pervade the picture; both cases harboured inflammatory masses—"orbital pseudo-tumours". So important did it appear in these cases that I am rather of the opinion that it may be a diagnostic feature.

Some reservation is necessary here, for another patient came to me because of pain in the distribution of the second division of the trigeminal nerve, with the diagnosis of "trigeminal neuralgia". He, at a later date, developed proptosis with full realization of the underlying disease—carcinoma of the maxilla. I may say that the original radiographs failed to indicate any difference between the two maxillæ. A similar case is presented in Dr. Dandy's series.

Tumour formation.—Apart from the formation of a mass superficially placed in the orbital outlet, it is unusual for any localized orbital swelling to attract the attention of the victim. More likely is it that a patient will be directed to the surgeon on account of increasing protrusion in the frontal or temporal region due to an underlying meningioma, or other pathological entity. Two patients of my series had had biopsies carried out on such temporal protrusions prior to my seeing them; one of these became infected in consequence, in fact it was the severity of the infection that led to his transfer. Occasionally one is able to feel the anterior margin of a mass tracking over the surface of the eyeball.

Alternative symptoms.—In addition to the above and more common complaints, various other symptoms have been responsible for the appearance of patients: amongst these symptoms may be mentioned ptosis, œdema of the eyelids, chemosis, cranial nerve palsies, an audible bruit, or a discharging sinus. While these symptoms obtrude as direct indicators of orbital involvement, tumours involving the orbit secondarily show in addition the associated clinical signs of their primary origin.

Malformations or erosions of the orbital walls, as from congenital deformities or mucocoeles respectively, should be recognizable by their contour and associated radiographical outlines, e.g. the frontal sinus.

When proptosis exists in association with generalized bone disease, the other affected regions of the skeleton will also be subjected to X-ray investigation. By these means the nature of the disease will be diagnosed.

Laboratory investigation.—In so far as investigations of a pathological nature are applied to problems in general I propose to make no especial comment. It is worthy of note, nevertheless, that in no case should operation be carried out for a presumed tumour without a W.R. or Kahn test.

Lumbar puncture may prove of value, both from manometric estimations of C.S.F. pressure and for analysis of the cerebrospinal fluid. In the extension of an optic nerve tumour through the optic canal, an increase of the total protein content of the cerebrospinal fluid may indicate that the subarachnoid space is involved. It may be possible, too, to differentiate between tumours by a like investigation, e.g. a mass is considered to occupy the middle fossa as well as implicating the orbit, is it meningiomatic or of a dermoid nature?—under the circumstances a rise of total protein content of the C.S.F. would favour the former.

The manometric pressure of the fluid, if above the normal, might indicate the intracranial extension of a tumour, although this means of anticipating such a state would not be without risk.

Treatment.—Having considered the patient from the general point of view and having reached the decision that operative intervention is the correct course, there is the question of the best route of approach. Excluding superficial lesions at the orbital outlet which can be dealt with adequately through the lids or the conjunctival sac, there remains the choice between an operation by the Krönlein approach, or a modification of it as described by Crawford, King and Rodgers, and the transfrontal exploration described by Dandy. My opinion concurs absolutely with that of Dr. Dandy in that the transfrontal route is preferable in every way (fig. 3). Through a frontal osteoplastic flap a more direct and more adequate exposure is obtainable, any extension intracranially is approachable, less interference with ocular mobility ensues, and there remains no visible and ugly scar. As for the replacement of a prominent eye by one that in addition pulsates, this is untrue. It is claimed by some that the risk of the operation is greater than by other routes, this also is not borne out when the operation is carried out by a trained neurosurgeon.

Obviously the occurrence of active infection precludes radical intervention. This complication will require the adoption of conservative measures, or the institution of suitable means of drainage. Some more radical form of surgical attack will then prove necessary on a subsequent but delayed occasion.

Rarely it may prove necessary, in control of infection, to eviscerate the eye. It is said that excision of the globe precludes exploration by the transfrontal route owing to the exaggerated risk of meningitis, but such is not the case when there is an adequate interval between the two procedures.

MATERIAL FORMING THE BASIS OF THE PAPER

	Group 1	Group 2	Group 3
Cyst—simple	1	1	3
Dermoid	—	1	2
Fibroma	1	—	—
Granuloma	1	—	3
Hæmangioma	—	4	1
Lacrimal gland tumour	—	1c	1
Meningioma	11	—	1+
Mucocoele—frontal	—	1	2
Ethmoidal	—	—	1
Optic nerve tumour—Glioma	—	21	3
Meningioma	—	—	1
Osteoma	2	—	—
Osteomatous cyst	1	—	—
Schüller-Christian disease	5	—	—
Chiasmal glioma	4	—	1
Lipoma	—	1	—

Group 1: Cases of Dandy.

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c indicates that the tumour was carcinomatous.

Although one case of meningioma is included within the present author's series, it is there purely as representing a type of case. The plus sign indicates that the author has had a number of such cases. Other cases of this type are not included, as they are not truly representative of "orbital tumours".

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Pathology.—A recapitulation of all the tumours to be found affecting the orbit would absorb much time, but give little help to our present deliberations. It is with this in mind that one decided to keep to the material at hand and to sort out from it some details requiring clarification. A striking point to my mind, when comparing the three basic series, is their lack of similarity: Dr. Dandy's commonest lesion is in reference to manifestations of "Schüller-Christian disease", Iles' and Rendle Short's paper reports four cases of "hæmangioma", and my own series provides four optic nerve tumours and three orbital pseudo-tumours. The main indication to be read from these findings is the failure of any small collection of cases to conform with the general perspective, and the annulment of that present-day attitude of rushing into the press with records of one or two cases. Another difficulty is the interpretation of the pathology, especially does this refer to "Schüller-Christian disease" and to "pseudo-tumour of the orbit". As I read Dandy's descriptions there would appear to be one case only where any xanthomatous tissue occurs and in which an alternative diagnosis is not available. There is one case in my own series upon which a biopsy was carried out elsewhere, and in the histological report is the following comment: "I would suggest that this is some sort of granuloma. Whether it is associated with a generalized metabolic disorder such as Schüller-Christian's disease one cannot say, although the history might guide one." A section of the tissue removed at operation leaves no doubt that the tumour is of "dermoid" origin (fig. 2, A, B and C). Some of the conditions described as "Schüller-Christian" deposits would appear to simulate the tissues of what, in my series, constitute the "pseudo-tumours" (fig. 5). It is of particular interest that one of the cases of hæmangioma recorded by Iles and Rendle Short had a nevus of the eyelid.

Tumours originating within the eye obviously belong to the realm of the ophthalmic surgeon. What is considered to be the correct treatment for a retinoblastoma that has extended along the optic nerve, in view of the comment of Verhoeff (1922) that retinoblastomas are the only known neoplasms of glial origin which metastasize to distant parts?

Tumours of the optic nerve have been fully investigated by the ophthalmic surgeons, particularly Hudson (1910) and Mathewson (1930). These two observers collected no less than 211 cases comprised as follows: 170 gliomata or 80.56%; 33 meningiomata 15.56%; 8 fibromata 3.8%.

Thus the incidence of glioma is between five and six times that of meningioma. Glioma is certainly a disease of the young: Hudson showed that 75% occur within the first decade, and that the average age of patients suffering from these tumours is 13 years. It is odd to find that Parsons (1942), in referring to optic nerve tumours, comments that "most of these tumours are probably endotheliomata which have undergone degeneration". In the collection of cases under review there are but four tumours arising from the optic nerve, and these are from one of the three series. Three of the tumours proved to be gliomas and were removed from children of 4½, 8, and 11 years of age. The fourth case, a meningioma, was in a patient of 33 years, who developed multiple intracranial tumours in association with generalized neurofibromatosis.

Radiographic examination.—The primary tumours restricted to the orbit generally show little X-ray evidence, perhaps an increase in bony density may be seen occasionally in the presence of the chronic inflammatory granulomata. Therefore unless a tumour is either of an invasive nature or extends beyond the precincts of the orbital cavity radiological verification, in all probability, will not be available. An osteoma, when present, casts such a dense shadow that it can hardly be controversial. Radiographic change takes on one of three forms: localized hyperostosis, sclerosis, or erosion. A localized hyperostosis is unusual in association with orbital implication, but may be seen in a meningioma of the olfactory groove. Sclerosis of bone is best seen with a meningioma of the sphenoid ridge. But of all appearances, changes of an erosive nature are most common, moreover they are very defined on account of the chronicity of the underlying lesion. The most impressive picture is that of an enlarged optic foramen brought about by intracranial extension of a tumour of the optic nerve. With an enlarged optic foramen the contour is important, and not just an increase in size; the dilated foramen must not be of an increase in one diameter alone; it should be circular rather than ovoid, or of other conformation indicating general distension. One may well ask if the optic foramina are always symmetrical, and to what extent an optic foramen can be encroached upon without causing pathological change in the nerve? Investigations by Clegg (1936) showed that the two foramina are by no means invariably symmetrical, indeed symmetry is to be found in but 45% of skulls. He also came to the conclusion that should the optic canal be constricted so that one diameter becomes reduced to 2.8 mm. or less, a normal nerve cannot exist within it. In his investigation he found that skull deformity with optic nerve symptoms occurs twice as often as do optic nerve tumours.

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Meningioma	11	—	1+
Mucocoele—frontal	—	1	2
Ethmoidal	—	—	1
Optic nerve tumour—Glioma	—	11	3
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Osteoma	2	—	—
Osteomatous cyst	1	—	—
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Orbital Tumours

By S. P. MEADOWS, M.D.

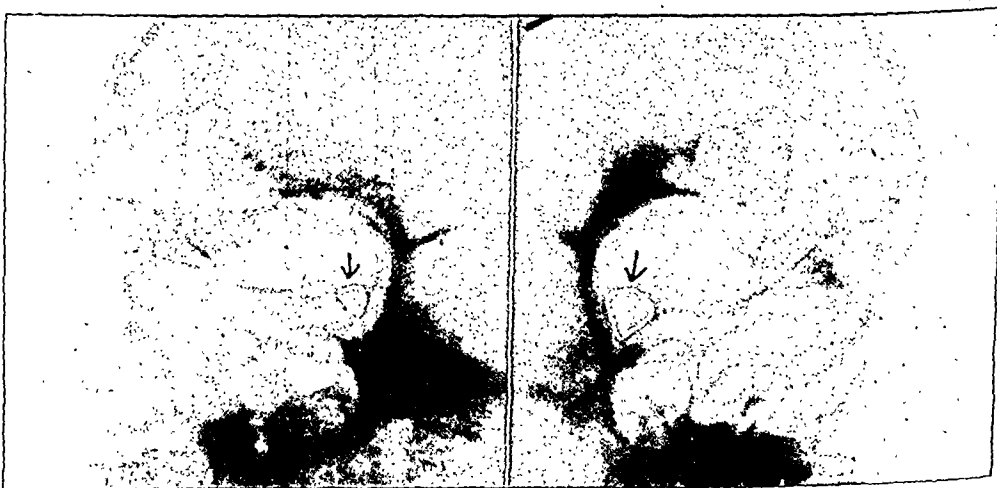
TUMOURS originating in, or involving the orbit by indirect extension, are of considerable interest to the physician, particularly with regard to diagnosis. Unfortunately it frequently happens that some cases are never proved by operation or otherwise, so that cases described are, in a sense, selected cases. Many so-called orbital tumours are not confined to the orbit. There is frequently an intracranial extension, which might be likened to the proverbial iceberg.

I should like to refer to a series of proved tumours involving the orbit seen personally during the past few years, some of them in the Physicians' Clinic at Moorfields Eye Hospital: I have chosen as representative cases: 1 glioma of the optic nerve; 3 meningiomas involving the orbit, one via the nerve sheath and two by hyperostosis; 1 venous tumour or angioma; 2 pseudo-tumours; 1 pituitary adenoma; 1 metastasis from carcinoma of the breast.

Several cases of carcinoma originating in the nasal sinuses and involving the orbit by direct extension have been excluded.

Glioma of the Optic Nerve

CASE I.—A girl, aged 15 years, with fifteen months' history of misty vision in the left eye, without pain or headache. Examination showed primary optic atrophy on the left side, visual acuity reduced to 6/60, and peripheral constriction of the visual field with loss of the lower temporal field and slight exophthalmos (4 mm.). Ocular movements were full. The left optic foramen was enlarged on X-ray examination (fig. 1).



Right optic foramen.

Left optic foramen.

FIG. 1 (Case I).—X-rays of optic foramina. (Glioma of optic nerve.)

On March 18, 1940, Mr. McKissock explored the orbit from above (intracranial approach). The optic nerve was enlarged as it joined the chiasm, and on removal of the orbital roof, the nerve was enormously enlarged as it was traced forwards, but became smaller again before it entered the globe. The nerve was excised, the eyeball being left intact. Microscopy of the tumour showed it to be a glioma, and the distal end of the nerve was normal.

The patient was quite well when last heard of, over four years after the operation.

This patient shows the essential clinical features of an intrinsic glioma of the optic nerve. These tumours are rare, only a few hundred being described in the literature. There is a slowly progressive unilateral visual loss in a young person, usually under 20 years of age, followed by gradually increasing exophthalmos, but little, if any, defect of ocular movement. Pain is usually absent. The fundus shows a primary optic atrophy.

and the optic foramen is enlarged on X-ray examination. The latter indicates an intracranial extension.

These tumours spread through the optic foramen up to, or even involving, the chiasm, and cases have been described where the tumour has spread as far as the hypothalamus over a number of years. The glioma may even spread to involve the opposite optic nerve. These tumours are occasionally seen in connexion with von Recklinghausen's neurofibromatosis, though they have no true relation with the latter. Microscopically they are similar to cerebral gliomas, but have a special picture, with marked polymorphism of cells, resembling some of the gliomas of the brain-stem and corpus callosum.

Meningiomas

These comprise one sheath meningioma (with intracranial extension) and two meningiomas with bony involvement of the orbit (hyperostosis). All occurred in women in the fifth decade.

CASE II.—Meningioma of the optic nerve sheath: Mrs. B., aged 41, presented with progressive failure of vision of the right eye of seven years' duration, without pain or headache. The right eye was almost blind within a year of the onset of symptoms. For two years there had been a progressive right exophthalmos, with aching pain in the right side of the head. Examination showed marked right exophthalmos, with visual acuity reduced to perception of light in the right eye. Ophthalmoscopic examination revealed optic atrophy with tortuous new vessels over the lower part of the right optic disc, and a patch of choroidoretinal atrophy in the upper nasal retina. Ocular movements were slightly limited in all directions on the right side, probably due to the exophthalmos, and there was no ptosis. The right pupil was fixed to direct light but reacted well consensually. A definite, though faint, systolic bruit was audible over the right eye at one time. X-ray examination showed enlargement of the right optic foramen.

At operation (right transfrontal exploration) a large meningioma ($4 \times 3 \times 3$ cm.) was found attached in the region of the right optic foramen, and along the optic groove and inner third of the sphenoidal ridge (fig. 2). Intraorbital extension of the tumour occurred along the optic canal, the optic nerve being surrounded by a cuff of tumour filling the subarachnoid space. The tumour filled most of the orbit. Complete removal of the intracranial portion was followed by excision of the orbital extension, after removal of the roof of the orbit and optic canal. The optic nerve was divided intracranially and near the globe.

On clinical grounds, before operation, this case would fit in with a sheath meningioma, and yet the orbital tumour was merely a part of a large, yet symptomless, intracranial meningioma. Without denying the existence of a sheath meningioma as a separate entity, it seems likely that many sheath meningiomas arise primarily in the intracranial cavity from the anterior cerebral meninges, e.g. sphenoidal wing, tuberculum sellæ, or in the parasellar region.

Thus it appears that in both glioma of the optic nerve and sheath meningioma one can never be sure pre-operatively that the intra-orbital portion of the nerve is the only part involved by the tumour.

The differential diagnosis of glioma from meningioma of the nerve may be summarized as follows: (1) Age of patient: Glioma under 20 years, meningioma in middle age. (2) Exophthalmos may occur before visual failure in meningioma. Visual failure is the first sign in glioma, and may be so in meningioma. (3) Oculomotor palsy, if present, suggests meningioma. (4) Pain is more common in meningioma. (5) Signs of intracranial extension may be present in meningioma.

CASE III.—Meningioma with hyperostosis of orbit: Mrs. P., aged 44, had had periodic generalized headaches for twenty-four years. For one year there had been protrusion of the right eye, and for six months swelling in the right temporal region. Examination showed a large diffuse swelling in the right temporal region, with slightly irregular surface, raised from the surface to the level of the zygoma, and about 2 in. in circumference. There were a few pulsating arteries palpable over the tumour. There was marked right exophthalmos (R. 28.5, L. 16.5, or 12 mm. exophthalmos), with slight limitation of all ocular movements, especially elevation (fig. 3). The right visual acuity was reduced to counting fingers, but the optic fundus and disc were normal. There was a defect in the lower right visual field with involvement of fixation, the upper periphery of the field being relatively intact. There were no other abnormal signs in the central nervous system, and, in particular, no anosmia.

X-ray examination (fig. 4) showed a diffuse opacity involving the walls of the right orbit, and spreading backwards to the temporal region. A portion of bone removed from the temporal region showed meningiomatous invasion of the bone (fig. 5). Operation was not undertaken.

CASE IV.—A similar case, a woman aged 40, with two or three years' history of right exophthalmos, with good vision and no pain. Examination showed right-sided exophthalmos of moderate degree as the sole physical sign, with normal vision, optic fundus and ocular movements. X-ray examination showed bony involvement of the orbit very similar to the preceding case.

The last two cases exhibit the clinical features of hyperostosis of the orbit due to meningioma, with exophthalmos preceding any loss of vision, and oculomotor palsy being late in onset or absent. These tumours may be very slow-growing and of many

years' duration. In some cases there is merely a small tumour or meningioma *en plaque*, with tremendous bony reaction or invasion, which may make radical extirpation very difficult or impossible.

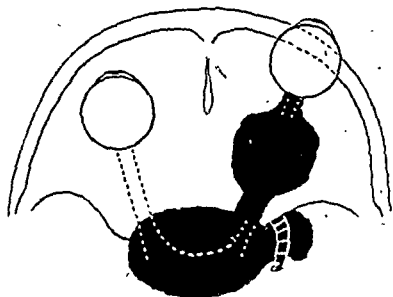


FIG. 2 (Case II).—To show extent of meningioma.

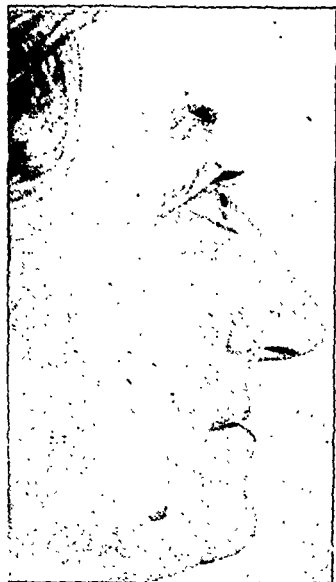


FIG. 3 (Case III).



FIG. 4 (Case III).—Hyperostosis and sclerosis of right orbit.

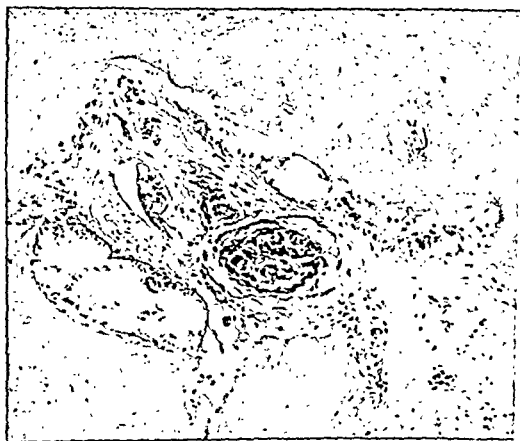


FIG. 5 (Case III).—Invasion of temporal bone by meningioma.



FIG. 7 (Case VI).—To show lid retraction, exophthalmos and chemosis.

CASE V.—*Venous tumour of the orbit*: A male, aged 45, gave a history of protrusion of the right eye on stooping. There was no pain, head noises, or disturbance of vision. Examination showed deep eye sockets, particularly on the right side, and especially above the upper lids. There may have been a localized lipodystrophy in this situation. There was no exophthalmos when the patient's head was upright or horizontal. the

exophthalmometer readings being R. 12 mm. and L. 14.5 mm. The right eye was slightly sunken at rest, suggesting a small bulk of orbital contents. When the patient stooped with head downwards, or on compression of the right jugular vein with the patient erect or lying down, the right eye rapidly became proptosed to no less a degree than 13.5 mm. (exophthalmometer reading 25.5 mm.). In addition the temporal fossa became fuller (fig. 6). There was no cephalic or ocular bruit, and no change in the fundus appearance when the eye was fully proptosed. Visual acuity was reduced from 6/12 with the eye at rest, to 6/18 with full proptosis.

This venous tumour of the orbit could thus be rapidly filled and emptied, and presumably communicated widely with the cavernous sinus. It did not interfere with the patient's activities, and no surgical treatment was undertaken.

Pseudo-tumour of the Orbit ("Fibromatosis of the Optic Nerve Sheath")

The following two cases are examples of the so-called pseudo-tumour of the orbit. In this condition, the aetiology and pathology of which we know little, the orbital tissue is replaced by a growth of dense fibrous tissue infiltrated with chronic inflammatory cells.



FIG. 6 (Case V).—Venous tumour of orbit: before and after compression of internal jugular vein.

The mass usually surrounds and may be intimately fused with the dural sheath—but does not invade the nerve itself—and with the sheaths of the enveloping ocular muscles. There is some doubt whether the pseudo-tumour arises from the sheath of the nerve. Endarteritis is said to be common in the tumour, which contains scattered lymphocytic foci. It appears to be of inflammatory origin, and may be syphilitic. The following two cases suggest the possibility of an endocrine origin, linking the condition with Graves' disease. Sarcoidosis may also be a possibility in some cases.

CASE VI.—R. S., male, aged 37, presented with right-sided exophthalmos of nine months' duration, without pain, but with occasional diplopia and blurring of vision. He had felt nervous recently and had lost weight. Examination revealed gross unilateral exophthalmos (12 mm.), the eye being also displaced downwards slightly. There was marked retraction of the upper and lower lids on the same side, and impaired elevation and abduction of the eye (fig. 7, p. 20). The visual acuity was 6/12 partly and the field full. In addition, the other eye showed a variable lid lag, and slight weakness of abduction. There were no definite general signs of thyrotoxicosis, except tachycardia (80-100), the B.M.R. was normal, and the thyroid gland not enlarged.

It was considered that the case was one of exophthalmos of Graves' disease, especially in view of the lid retraction. The appearance of papilloedema and loss of corneal sensation in an essentially unilateral abnormality made us doubt this diagnosis. The patient refused operation until there was a large corneal ulcer, and the eye almost blind.

The right eye was excised, and during the operation a firm yellowish tissue was seen behind the eye. About three weeks later the orbit was exposed from above (right frontal flap and decompression of the orbit). On opening the periosteum of the orbit, a large hard ovoid tumour was seen, attached posteriorly and anteromedially, and was removed intact. The optic nerve appeared to be surrounded by the tumour. The tumour was 2½ cm. long and 1 cm. thick, and contained a central white core, presumably the remains of the optic nerve.

Microscopy of the tumour showed intense lymphocytic infiltration, with some plasma cells and probably some polymorphs, with oedema, secondary fibrosis, and degeneration of muscle fibres of the extrinsic muscles. The oculomotor nerves appeared normal.

The patient has remained well for nearly three years after the operation, and the remaining eye is normal.

[This patient was shown at a meeting of the Clinical Section, before operation, as a case of exophthalmic ophthalmoplegia, *see Proc. R. Soc. Med.*, 1941, 35, 12.]

CASE VII.—W. S., male, aged 56, had unilateral exophthalmos of three months' duration, without pain, headache, or loss of vision. Examination showed right exophthalmos (9 mm.), with no horizontal or vertical displacement. There was intense conjunctival injection and chemosis, and the globe was tender on pressure and could not be pushed back. There was defect in all ocular movements, especially elevation, but no lid retraction. The right pupil reacted sluggishly to light. At a later stage the patient developed severe pain in the right eye, and V.A. was reduced to 6/60. The corneal reflex became diminished and a corneal ulcer developed. The optic fundus remained normal. There was no clinical evidence of thyrotoxicosis, though the B.M.R. was +34% on one occasion. In view of the unilateral exophthalmos and the absence of lid retraction, and the fact that the globe could not be reduced by pressure, a diagnosis of orbital tumour was made. Decompression of the orbit from above (intracranial approach) was undertaken by Mr. McKissock, and a large hard mass of tissue was removed from beneath the superior rectus muscle, to which it appeared to be attached. The optic nerve was not seen. The tumour measured 1 cm. long, 1 cm. wide, and $\frac{1}{2}$ cm. thick. The ptosis was reduced by operation, but the cornea later perforated and the eye had to be eviscerated. The histology was that of a pseudo-tumour (*see Mr. Goldsmith's remarks later*).

This case has an interesting sequel, for fourteen months after the operation on the right eye, the remaining eye became similarly affected. The left eye was proptosed, and there was well-marked chemosis, and bulging of the upper and lower lids. There was no lid retraction, but ocular movements were limited in all directions, especially abduction. The retinal veins were engorged but there was no papilloedema. The visual acuity was 6/12 and corneal sensation was normal. There were no clinical signs of thyrotoxicosis. There was, in addition, a mass palpable in the old socket. The patient refused operation on the remaining eye, which developed a corneal ulcer.

These two cases are of considerable interest, particularly in the differential diagnosis from the exophthalmos of Graves' disease. In the first case there was lid retraction and the condition was at first attributed to endocrine disorder, and in the second case both eyes were affected. It may be, of course, that these cases are allied to Graves' disease, and that the condition is a form of exophthalmic ophthalmoplegia.

CASE VIII.—*Orbital metastasis*: This patient is described in view of the fact that a proved orbital metastasis from a carcinoma of the breast was known to have been present for at least six years.

The woman, aged 60, had noticed unilateral ptosis when she was in hospital six years previously for removal of a carcinoma of the breast. She later presented with a third nerve palsy and pain above the eye, of two years' duration. There was no definite exophthalmos. At autopsy the soft tissues of the orbit contained deposits of adenocarcinoma, with invasion of fat, muscle, and nerves.

CASE IX.—*Pituitary tumour*: This patient, a male, aged 24, had been blind for three years when first examined. Six years previously he had developed progressive deterioration of vision in both eyes, and later developed severe frontal headaches. Bilateral exophthalmos had slowly appeared over a period of four years, with increasing obesity and change in features.

Examination revealed advanced bilateral optic atrophy, with blindness, and pupils which were fixed to light. Ocular movements were full. There was very marked bilateral exophthalmos (Hertel R. 24, L. 27) and the left eye showed definite pulsation. There were mild acromegalic features in the face and hands. An X-ray of the skull showed complete destruction of the sella turcica, and the optic foramina and ethmoids had disappeared. In view of the latter, it seems likely that the exophthalmos was of mechanical origin due to invasion forwards by the pituitary tumour.

It seems likely that, as orbital tumours are uncommon, no one observer sees a sufficient number of cases to appreciate the relative frequency of the different pathological types. Each variety of tumour probably has its own clinical characteristics. A large proportion of these tumours extend into the cranial cavity, or are forward extensions of an intracranial mass.

Progressive unilateral exophthalmos, usually painless, is a common presenting symptom, though visual failure may precede this if the tumour is inside the muscle cone. The exophthalmos may be axial, or the eye may be displaced vertically. In one case of this series, a meningioma, an orbital bruit was heard on one occasion, and in another, probably a forward extension of a pituitary adenoma, the exophthalmos was definitely pulsatile. Chemosis and conjunctival congestion are seen in the later stages. Resistance to backward pressure on the front of the globe is probably an important point in diagnosis, and the anterior margin of the tumour may occasionally be palpated round the globe. The bone of the peri-orbital region may be involved by the tumour (Case III).

Loss of vision followed by optic atrophy is, of course, a common finding where the tumour involves the optic nerve. The visual field may show a central defect spreading to involve one part of the periphery (Case III). In many cases, however, and particularly when the tumour originates outside the muscle cone, vision is retained, or visual loss occurs late in the history. Papilloedema was found in only one case of the present series, a pseudo-tumour, probably originating within the muscle cone, and was a late feature.

Lid retraction is probably a rare accompaniment of orbital tumour. It occurred in one case of the present series, a pseudo-tumour. Ptosis is more likely to occur than lid retraction, and the latter is, as a rule, a diagnostic pointer to the exophthalmos of Graves' disease.

It is surprising how little defect there is in ocular movements in some of these cases, e.g. Case II, where the orbit was almost filled with meningioma. Ocular palsy, or marked defect in ocular movements, is probably a late sign in many cases. In metastatic orbital tumours a third nerve palsy is fairly common, however (Case VIII).

Involvement of the ophthalmic division of the trigeminal nerve was not seen in this series of cases. If it is affected it probably points to an intracranial extension of the tumour. Ocular sympathetic involvement probably accounts for the small pupil in some cases of third nerve palsy of metastatic origin, but this feature is perhaps more common in intracranial aneurysms of the carotid artery.

I am indebted to Dr. Russell Brain for permission to publish Case II.

Mr. A. J. B. Goldsmith: Orbital pseudo-tumours were first described by Birch-Hirschfeld some forty years ago and the term has been held to connote a slowly-developing exophthalmos associated with a non-mycotic infection. Most writers have adhered to Birch-Hirschfeld's original classification dividing the condition into three groups. In the first the disease is clinically a tumour, without evidence of tuberculosis, syphilis or blood or other disease, but subsiding on treatment with mercury, arsenic or iodides. This is unsatisfactory from the pathological point of view, as, although the patient may be cured, there is no certainty as to the underlying basis.

In the second group, at operation, what is thought to be a tumour is removed, but on pathological examination this is found to consist of fibrotic chronic inflammatory tissue only.

The third group is similar to group 2, but in addition lymphoid follicles are also present.

In the light of more recent knowledge many pseudo-tumours must be considered as probably unilateral thyrotrophic exophthalmos. One of these is described by Birch-Hirschfeld, a man in whom one orbit was exenterated for a presumed sarcoma, but the tissues showed what was called chronic inflammatory tissue only. After operation the other eye became markedly proptosed and remained so for some years, then returning to its normal position.

Other cases described, such as the first in Dandy's book on orbital tumours, and one described by Dalsgaard-Nielsen, have presented nodules outside the muscle cone, which have shelled out readily, and their removal has led to complete recovery. Pathologically both these showed chronic inflammatory fibrous tissue infiltrated by lymphocytes but without lymphoid folliculosis, in other words belonging to group 2 of Birch-Hirschfeld's classification.

In two cases both operated on by Mr. McKissock, the diagnosis, based on the operative and pathological findings, was of pseudo-tumour. In the first the pathological material showed chronic inflammatory fibrous tissue infiltrated by lymphocytes without follicles. It was part of a mass removed from a socket, the eye having been lost by corneal ulceration by exposure from displacement forwards by the mass.

In the second case a tumour-like mass was present in the inner and upper part of the orbit involving the superior oblique muscle. This mass was encapsulated and was easily shelled out and removed complete after dividing the two ends of the affected muscle. No other mass was felt in the orbit at the end of operation. On section of the tissue removed it was found to consist of oedematous muscle showing necrosis of fibres, much fibrosis, lymphocytic infiltration and many lymphoid follicles, the whole being surrounded by a fibrous capsule. Thus looking at the fibrosis the case would fall into group 3 of Birch-Hirschfeld's classification, but the changes in the muscle are similar to those described by Mulvany as occurring in thyrotrophic exophthalmos. In view of the complete localization of the mass we labelled the condition as pseudo-tumour, but the subsequent history is interesting. The cornea had ulcerated from exposure and had perforated before the orbital exploration. After operation the ulceration spread and the eye had to be removed. The socket healed well and was quite soft, but I understand that the patient has recently, some eighteen months after removal of the mass and of the eye, developed another mass in the anophthalmic socket, and has also proptosis of the other eye, suggesting that he has been all along an anomalous case of exophthalmic ophthalmoplegia.

It is possible that in some cases of thyrotrophic exophthalmos the pathological changes may for some time remain confined to one muscle or contiguous muscles, usually the superior rectus and oblique. Some of the cases in the literature falling into group 3 pseudo-tumours may in fact be of this type; though frequently the pathology and subsequent clinical course have not been sufficiently detailed to afford any enlightenment on this point.

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Mr. R. Affleck Greaves said that when a retinoblastoma was found to have invaded the central end of the severed optic nerve, he thought the usual practice would be to employ radiotherapy. He remembered, however, a case reported by Mr. Norman Dott in which the skull was opened and the intracranial part of the nerve removed, with a completely successful result. Cases of optic nerve involvement were fortunately very uncommon.

The speaker thought the textbooks were correct in stating that dermoids were most often situated anteriorly, but agreed that they might be retro-ocular and so cause proptosis. He quoted a case of his own, which as far as he knew was unique, in which a retro-ocular dermoid was found to be fixed to the outer wall and roof of the orbit by an encasing thin bony capsule. The original diagnosis made on the strength of the X-ray picture was that of enchondroma.

Though pain was a rare symptom in cases of orbital tumour, if it did occur, especially in the early stages, it suggested that the tumour was probably of a malignant nature. He had observed that in cases of metastasis in the apex of the orbit from breast cancer a fifth nerve neuralgia was apt to precede the onset of appreciable proptosis.

With regard to the two cases of pseudo-tumour quoted by Dr. Meadows, he had little doubt in his own mind that these were actually cases of Graves' disease, and he thought that the microscopic findings threw an interesting light on the possible causes of exophthalmos in association with that condition. One variety of pseudo-tumour was a localized periostitis of the orbital wall and in such cases it was his experience that the exophthalmos subsided in time, though the process was extremely slow.

It was important to remember that tumours consisting of lymphoid tissue occurred in the orbit, especially in cases of leukaemia and allied diseases of the lymphatic system, and that a blood-count might reveal the nature of an orbital tumour.

Mr. A. Dickson Wright said that his personal series of orbital tumours differed from those recorded by the opener. They consisted of four lacrimal tumours, one optic nerve glioma and no less than five true meningiomas of the optic nerve sheath. As regards the lacrimal tumours they were all now dead from recurrences of different kinds, one in the liver only and the others in the cranial bones, this in spite of the clean removal and intensive post-operative radiation. These tumours, although histologically the same as parafid tumours, had a most evil prognosis.

After removal of the optic nerve with its glioma in the one case of a child, phthisis bulbi had resulted whereas in the optic sheath meningiomas the eye had retained its shape and appearance after removal of the optic nerve. Squints were usual, but in one case a satisfactory operative correction had been made. An interesting point was that these tumours grew outwards from the sheath which after removal could be slid up and down on the nerve proper. This had prompted the speaker in his last case to remove the tumour by morcellement and then the portion of sheath was removed, leaving the bare nerve for a distance of a centimetre in the hope that vision might be preserved. This was not achieved but it might be a possibility in earlier cases.

Another important orbital tumour was provided by intra-orbital extension of the creeping carcinomas of the nasal passages and sinuses, the so-called epithelioma terebrans. The combination of one-sided nasal obstruction and epistaxis with exophthalmos and deafness on the same side made a very clear syndrome. No surgery, possibly not even biopsy, should be attempted as most encouraging results were obtained by thorough radiation of the whole area.

As regards the pseudo-tumours which have a tendency to resolve spontaneously might they not be a form of Boeck's sarcoid, possibly best treated by orbital decompression rather than removal which generally seemed to cause loss of vision?

[February 1, 1945]

Acroparæsthesia. [A Summary].

By SIMON BEHRMAN, M.R.C.P.

THE manifestations of this syndrome were first accurately described by Ormerod in 1883 and they can be summarized as follows:

(1) Symptoms: (a) are confined to upper extremities; (b) comprise paræsthesiæ (peripheral in distribution), often associated with pains of radiating type; (c) are most pronounced on awakening; (d) when present during the day, they are brought on by manual activities of a certain kind.

(2) There is usually a paucity of abnormal physical signs.

(3) The syndrome: (a) usually runs a chronic fluctuating course; (b) is usually relieved by rest and aggravated by work; (c) is met with chiefly in women in the later years of life.

This syndrome is met with either independently or in association with pregnancy, acromegaly and Pager's disease. Several cases of acroparæsthesia in the male were described.

Pregnancy acroparæsthesia deserves special attention since it is a fairly common condition, particularly minor degrees of it. In the past it seems to have been regarded as an incomplete form of pregnancy neuritis and, as such, attributed to nutritional and dietetic causes. Symptoms usually arise during the second half of pregnancy and most frequently occur with the first pregnancy. There is usually a dramatic improvement immediately after delivery, but symptoms frequently return after the patient has resumed her household duties, when they may become even more intense than during the pregnancy. A large proportion of women showing this condition develop it in the course of the first pregnancy and are not troubled with it in subsequent pregnancies. On the

other hand, a multiparous woman who, after a normal first pregnancy, develops acroparæsthesia in the course of any other pregnancy, is very likely to be so troubled with every subsequent pregnancy.

Various theories which, in the past, have been proposed to explain acroparæsthesia, such as "vasomotor neurosis", endocrine dysfunctions, &c., were reviewed and found unsatisfactory.

A mechanical pathogenesis was put forward, the view being based on the following arguments: (1) There is evidence to suggest that the disorder of function is affecting the peripheral nervous system of the arms. This is indicated by (a) the restriction, even in most advanced cases of long standing, of all the symptoms to the upper extremities; (b) the presence of objective sensory disturbances at the periphery in some cases; and (c) evidence in some cases of increased mechanical irritability of the nerves of the arm.

(2) Since, in the majority of cases, the sensory disturbances are present in all fingers, it can be inferred that the spinal nerves composing the brachial plexus, or the brachial plexus itself, are principally involved.

(3) In view of the fact that acroparæsthesia is invariably relieved by rest and aggravated by muscular effort involving the shoulder girdle and upper extremities, it is probable that this lesion is mechanically determined.

When considering the possible causative mechanical factors, the important influence of sex and age on acroparæsthesia must be recognized. Evidence was adduced that these differences of sex and age tend to bring about a diminution of downward and forward obliquity of the superior aperture of the thorax; a downward descent of the shoulder girdle as a whole may also take place as a result of senescence. The resulting change in the relations of the structures would favour some degree of compression of the elements of the brachial plexus, especially in those cases where certain developmental abnormalities are already present. The neck muscles, by their contraction, probably contribute their quota to the "overcrowding" of structures in this region. When the arms are employed in certain actions, such as knitting, typing and writing, &c., the shoulder girdle has to be fixed and the neck muscles are utilized for this purpose indirectly. They may remain in a state of contraction for some time and this is probably sufficient, under the abnormal circumstances prevailing, to produce some physiological disturbances in the brachial plexus and thus give rise to paræsthesia. In man, these muscles are, in addition, concerned to an important extent in aiding the diaphragm in respiration. Given, therefore, conditions favouring thoracic breathing, a persistent activity of these muscles will follow. The predominantly thoracic breathing occurring during sleep might explain the symptoms present on awakening in acroparæsthesia. It must be added, however, that in a typical case of acroparæsthesia in which tenotomy of the scalenus anticus was performed on one side, no unequivocal improvement resulted.

According to the view put forward, a concatenation of a number of different anatomical (congenital and acquired) and physiological factors can produce the syndrome of acroparæsthesia; common to all cases, however, is a slight compression of the brachial plexus, usually only of a degree sufficient to bring on transient symptoms, but insufficient to produce any irreversible damage.

The Anatomy of the Thoracic Outlet in Relation to "Irritation" and Compression of Nerve Trunks

By G. WEDDELL, M.D.

Department of Anatomy, University of Oxford

Introduction.—The morbid anatomy of the thoracic outlet which may lead to a compression or angulation of the brachial plexus is complex and due to a number of different factors. There has been a tendency recently somewhat to oversimplify the aetiology of neurological symptoms and signs resulting from abnormalities of the thoracic outlet. For instance, in a paper by Swank and Simeone (1944), cases with neurological symptoms and signs known to have cervical ribs are included under the heading of "scalenus anticus syndrome", whereas properly speaking, this term should be reserved for cases in which abnormalities of the scalenus anticus muscle are the primary cause of the affection. There is a danger that this form of oversimplification will lead to less precision in diagnosis, and thus mismanagement of treatment. Whenever neurological symptoms or signs consistent with compression or "irritation" of the brachial plexus are encountered, attempts should be made to establish a precise diagnosis in order that treatment should be rational.

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The relation of the brachial plexus to the thoracic outlet.—Jones (1913) has stated that from the phylogenetic point of view it is the formation of the brachial plexus which produces the ribless neck, and that from the embryological point of view anomalies in the limb plexuses are primary and not secondary to anomalies in the disposition of the ribs and vertebral elements. In a series of anatomical studies he has demonstrated, among other things, that when a brachial plexus includes caudal nerve roots which are normally outside the limits of the plexus the interference with the development of the first thoracic rib may be expected to reach its maximum. In contrast, when a cervical rib is well developed the plexus receives no contribution, or only a very small one, from the first thoracic nerve. He concludes that under normal conditions post-fixation of the brachial plexus may readjust itself with the rib elements at a lower level, so may pre-fixation of the plexus readjust itself at a higher level. It is in the intermediate grades, in which the development of the costal process is in excess of the plexus alteration, that strain is produced and symptoms are developed.

The cervical vertebrae.—The anatomy of cervical ribs (or fibrous bands related to them) is too well known to need description. In many instances (Adson and Coffey, 1927) relief of symptoms and signs due to their presence can be effected by division of the scalenus anticus muscle only. However, it is important to distinguish these cases as a separate group from those of the "scalenus anticus syndrome", for on occasions either the rib may be so disposed in relation to the nerve trunks that this procedure alone is not effective, or fibrous bands extending from the tip of the rib towards the first thoracic rib have to be divided in order to relieve the pressure.

In addition to cervical ribs there may well be abnormalities of the cervical vertebrae in the neighbourhood of the emergence of the nerve roots, such as osteophytic out-growths causing the slips of origin of the scalenus anticus muscle, during contraction, to compress the roots. Swank and Simeone (1944) have emphasized the close relationship between the tendinous slips of origin of the scalenus anticus muscle and the cervical nerve roots. Each tendon of origin passes directly in front of, and in close relation with, the cervical nerve root one segment below. The nerves pass laterally and slightly downwards in grooves on the antero-superior surfaces of the transverse processes of the cervical vertebrae. Near the tips of these processes, the nerve lies directly between the transverse process which is grooved for it to lie in, and the tendon of origin of the scalenus anticus muscle arising from the transverse process above.

The scalene muscles.—The "scalenus anticus syndrome" is now well recognized, Swank and Simeone (1944) have described three types: "superior", "inferior" and "mixed" according to the particular nerve roots involved. They believe that the mechanism is similar to that of a vice, the ventral jaw of which is the scalenus anticus muscle, the structure or structures forming the dorsal jaw varying in different cases. They believe that the aetiology is due to hypertrophy of the scalenus anticus muscle following overactivity of the respiratory muscles. Unfortunately, there is no proof that their assumptions are correct. In 4 of the 15 cases reported, the symptoms and signs subsided with heat and massage, and with head posture designed to rest the affected muscle. Of the 10 patients submitted to operation, after failure on conservative treatment, the scalenus anticus muscle was said to be hypertrophied but they give no details of the standard against which they made this judgment. Abnormalities of the muscle and cervical ribs, &c., were noted in 9 of the cases, but no mention is made of any manœuvres performed at operation to show the vice-like action of the muscle.

Relief of the symptoms, however, was obtained in all cases submitted to operation. It is certain, therefore, that division of scalenus anticus muscle was curative in that it relieved pressure from the nerve roots of the brachial plexus, but it is possible that the real aetiological factor lay primarily in the dorsal jaw of the vice, as in the cases of cervical rib, which they include under the heading "scalenus anticus syndrome". It is important to emphasize this point, for section of the scalenus anticus muscle for the relief of symptoms may not always be effective in cases of so-called "scalenus anticus syndrome". For instance, Falconer and Weddell (1943) have reported a case of compression of the lower trunk of the brachial plexus due to a tendinous band in the position of the scalenus minimus muscle. Clinically this case gave symptoms and signs typical of a "scalenus anticus syndrome". Cure was effected by division of the band. At operation the scalenus anticus muscle could not be made to compress any of the plexus nerve roots by stimulation of postural manœuvres, and was left intact.

Enough has been said to show that the nerves composing the brachial plexus may be subjected to compression or distortion at a number of points between their exit from the intervertebral foramina¹ and their entrance into the axilla. Anatomical and physio-

¹ Proapsed cervical intervertebral disc (Elliott and Kremer, 1945) must also be considered in the differential diagnosis in subjects with symptoms and signs of "irritation" or compression of the nerve roots composing the brachial plexus.

From the anatomical point of view, therefore, abnormalities in relation to the following structures should be considered.

THE MORRID ANATOMY OF THE THORACIC OUTLET

Descent of the shoulder girdle.—Todd (1912) has suggested that compression of the subclavian structures can result from an abnormal development of the shoulder girdle. He supposes that normally during the course of development and growth, the acromial end of the clavicle and shoulder descend because of the weight of the upper extremity, and the sternal end of the clavicle descends because of the contraction of the rectus abdominis muscle transmitted through the sternum. On the other hand, no symptoms occur unless there is abnormal descent of the shoulder, or an arrested descent of the sternum and the anterior ends of the ribs. Either one or both of these abnormalities may (according to Todd) result in compression of the subclavian structures because of the stretching of the brachial plexus and subclavian vessels over a fixed cervical or first dorsal rib. He has shown that the descent of the shoulder is greater in females than in males, and presumes that this is due to a less powerful development of the suspensory muscles of the shoulder, especially the trapezius. In addition, he argues that the rectus abdominis muscle is relatively less powerful in the female, and thus exerts less pull on the sternum with the result that the anterior extremities of the clavicle and ribs are fixed at a higher level. These arguments are consistent with the clinical observation that cases of cervical rib with neurological symptoms and signs are more common in females.

On the basis of Todd's discussion, it is to be expected that, in a certain number of subjects who show minimal morphological abnormalities of the thoracic outlet, symptoms and signs referable to compression or "irritation" of roots of the brachial plexus will not appear until they are exposed to unaccustomed strain. Such strain may take the form of carrying of heavy weights, or bearing heavy packs on the shoulders, leading to an over-stretching of the trapezius muscles and thus to an abnormal descent of the shoulder girdle. Murphy (1910), Stopford and Telford (1919) and others have described cases where symptoms of compression of the lower trunk of the brachial plexus by an apparently normal first thoracic rib, were relieved by removal of a segment of the rib. Geddes (1912) has also described a case in which symptoms related to angulation of the brachial plexus following pregnancy, were entirely relieved by postural manœuvres designed to elevate the shoulder girdle and increase the "tone" of the trapezius muscles.

Costo-clavicular compression.—Falconer and Weddell (1943) described three cases with symptoms and signs suggestive of a "scalenus anticus syndrome" which occurred following unaccustomed strain involving muscles of the shoulder girdle. The clinical picture was found to be due to an intermittent compression of the subclavian structures between the clavicle and the first rib. In these cases, morphological abnormalities resulting in an excessive narrowing of the interval between the clavicle and the first rib were responsible, and not angulation of the subclavian structures over the rib, or compression of the subclavian structures between the rib and scalenus anticus muscle. In one case in which symptoms and signs were unilateral there was radiographic evidence of asymmetry of the thoracic outlet. This patient was submitted to operation under local anaesthesia and proof was forthcoming during postural manœuvres with the structures exposed, that the subclavian structures were being compressed between the clavicle and first rib. Contraction of the scalenus anticus muscle, either voluntarily or when stimulated electrically, was without effect. Following the removal of a segment of the first rib the symptoms and signs disappeared and the subclavian structures were no longer compressed by postural manœuvres designed to approximate the clavicle to the first rib.

During the course of the operation an aneurysmal dilatation of the subclavian artery beyond the scalenus anticus muscle was encountered, proximal to the point of compression of the vessel. Similar aneurysmal dilatations have been described previously, and explained as being due to compression of the vessel between the first rib and the tendon of the scalenus anticus muscle. Ingenious theories have been evolved to account for the dilatation distal to the point of compression, but it appears probable that, in such cases, the chief point of compression of the vessel has been mistaken.

The first rib.—Abnormalities of the first rib alone may also give rise to symptoms of compression due to angulation of the lower trunks of the brachial plexus. For instance, Swank and Simeone (1944) state that the first thoracic rib may have an abnormal curvature. It is of some interest that "stress" fractures of the first rib, though rare, may occur in the neighbourhood of the subclavian groove (Alderson, 1944). Changes resulting from such fractures might well lead to symptoms and signs referable to compression or "irritation" of the nerves composing the brachial plexus.

The relation of the brachial plexus to the thoracic outlet.—Jones (1913) has stated that from the phylogenetic point of view it is the formation of the brachial plexus which produces the ribless neck, and that from the embryological point of view anomalies in the limb plexuses are primary and not secondary to anomalies in the disposition of the ribs and vertebral elements. In a series of anatomical studies he has demonstrated, among other things, that when a brachial plexus includes caudal nerve roots which are normally outside the limits of the plexus the interference with the development of the first thoracic rib may be expected to reach its maximum. In contrast, when a cervical rib is well developed the plexus receives no contribution, or only a very small one, from the first thoracic nerve. He concludes that under normal conditions post-fixation of the brachial plexus may readjust itself with the rib elements at a lower level, so may pre-fixation of the plexus readjust itself at a higher level. It is in the intermediate grades, in which the development of the costal process is in excess of the plexus alteration, that strain is produced and symptoms are developed.

The cervical vertebrae.—The anatomy of cervical ribs (or fibrous bands related to them) is too well known to need description. In many instances (Adson and Coffey, 1927) relief of symptoms and signs due to their presence can be effected by division of the scalenus anticus muscle only. However, it is important to distinguish these cases as a separate group from those of the "scalenus anticus syndrome", for on occasions either the rib may be so disposed in relation to the nerve trunks that this procedure alone is not effective, or fibrous bands extending from the tip of the rib towards the first thoracic rib have to be divided in order to relieve the pressure.

In addition to cervical ribs there may well be abnormalities of the cervical vertebrae in the neighbourhood of the emergence of the nerve roots, such as osteophytic outgrowths causing the slips of origin of the scalenus anticus muscle, during contraction, to compress the roots. Swank and Simeone (1944) have emphasized the close relationship between the tendinous slips of origin of the scalenus anticus muscle and the cervical nerve roots. Each tendon of origin passes directly in front of, and in close relation with, the cervical nerve root one segment below. The nerves pass laterally and slightly downwards in grooves on the antero-superior surfaces of the transverse processes of the cervical vertebrae. Near the tips of these processes, the nerve lies directly between the transverse process which is grooved for it to lie in, and the tendon of origin of the scalenus anticus muscle arising from the transverse process above.

The scalene muscles.—The "scalenus anticus syndrome" is now well recognized, Swank and Simeone (1944) have described three types: "superior", "inferior" and "mixed" according to the particular nerve roots involved. They believe that the mechanism is similar to that of a vice, the ventral jaw of which is the scalenus anticus muscle, the structure or structures forming the dorsal jaw varying in different cases. They believe that the aetiology is due to hypertrophy of the scalenus anticus muscle following overactivity of the respiratory muscles. Unfortunately, there is no proof that their assumptions are correct. In 4 of the 15 cases reported, the symptoms and signs subsided with heat and massage, and with head posture designed to rest the affected muscle. Of the 10 patients submitted to operation, after failure on conservative treatment, the scalenus anticus muscle was said to be hypertrophied but they give no details of the standard against which they made this judgment. Abnormalities of the muscle and cervical ribs, &c., were noted in 9 of the cases, but no mention is made of any manœuvres performed at operation to show the vice-like action of the muscle.

Relief of the symptoms, however, was obtained in all cases submitted to operation. It is certain, therefore, that division of scalenus anticus muscle was curative in that it relieved pressure from the nerve roots of the brachial plexus, but it is possible that the real aetiological factor lay primarily in the dorsal jaw of the vice, as in the cases of cervical rib, which they include under the heading "scalenus anticus syndrome". It is important to emphasize this point, for section of the scalenus anticus muscle for the relief of symptoms may not always be effective in cases of so-called "scalenus anticus syndrome". For instance, Falconer and Weddell (1943) have reported a case of compression of the lower trunk of the brachial plexus due to a tendinous band in the position of the scalenus minimus muscle. Clinically this case gave symptoms and signs typical of a "scalenus anticus syndrome". Cure was effected by division of the band. At operation the scalenus anticus muscle could not be made to compress any of the plexus nerve roots by stimulation of postural manœuvres, and was left intact.

Enough has been said to show that the nerves composing the brachial plexus may be subjected to compression or distortion at a number of points between their exit from the intervertebral foramina¹ and their entrance into the axilla. Anatomical and physio-

¹ Prolapsed cervical intervertebral disc (Elliott and Kremer, 1945) must also be considered in the differential diagnosis in subjects with symptoms and signs of "irritation" or compression of the nerve roots composing the brachial plexus.

logical abnormalities in relation to all parts of the following structures must be considered when making a diagnosis and instituting treatment: (1) The clavicle and first rib; (2) the brachial plexus; (3) the cervical vertebræ; (4) the scalene muscles.

It must always be remembered that a combination of abnormalities may be present.

The importance of exact diagnosis in relation to treatment.—If a number of the nerve fibres composing the brachial plexus have undergone Wallerian degeneration, the results of any form of treatment will be disappointing, for the regeneration of peripheral nerves, particularly over long distances, is functionally poor. Howell (1913) reviewed the results of operative treatment in cases with cervical ribs and concluded that, with regard to muscular weakness and atrophy, operation will greatly improve the condition if not too long delayed. It is, therefore, of the utmost importance that an exact diagnosis should be made early in cases of brachial plexus, "irritation" or compression. Careful clinical, radiographic, and electromyographic assessment of each case should be undertaken in order to determine the mechanism giving rise to the symptoms and signs. For instance, in cases of acroparesthesia associated with pregnancy, the symptoms are probably determined by anatomical changes occurring during the latter half of pregnancy. Respiration becomes more costal in type with consequent elevation of the first rib and is associated with increased activity and perhaps hypertrophy of the scalene muscles which leads to a narrowing of the thoracic outlet. Since the changes responsible for the symptoms are reversible, the treatment is clearly conservative. Similarly in cases with abnormalities of the thoracic outlet in which symptoms and signs have arisen as a result of a change in occupation (leading to a descent of the shoulder girdle) the treatment is conservative in the first instance. In the majority of such cases, the pathological changes are reversible, and cure may be expected to follow the removal of the precipitating cause of the affection. On the other hand, in all cases in which symptoms and signs are progressive despite conservative measures, operation should be undertaken early in order to forestall Wallerian degeneration.

Any operation undertaken should be regarded as exploratory, and should preferably be performed under local anaesthesia. During the course of the operation every attempt should be made, by postural manœuvres and electrical stimulation of the scalenus anticus muscle, to determine both the exact point and mechanism of the compression of the nerves. In some cases division of the scalenus anticus muscle alone will relieve the affection although its primary cause is a cervical rib. On other occasions it may be necessary to remove a segment of the first rib, or to divide a fibrous band occupying the position of a cervical rib.

Since this Address was given a paper has appeared in *Brain* by Walshe *et al.* (1944) entitled: "On some pressure effects associated with cervical and with rudimentary and 'normal' first ribs, and the factors entering into their causation." It is pleasing to note that our conclusions are in substantial agreement.

SUMMARY

(1) The anatomy of the thoracic outlet has been discussed in relation to "irritation" and compression of nerve trunks. (2) It has been emphasized that the nerves composing the brachial plexus may be subjected to "irritation" or compression at a number of points along their course, and that a number of anatomical and physiological factors may be responsible, either singly or in combination. (3) It is important to establish the precise nature of the anatomical conditions in the establishment of a diagnosis if treatment is to be successful. (4) In cases in which symptoms and signs are progressive, operation should be undertaken as early as possible. Exact confirmation of the diagnosis should be obtained at operation by postural manœuvres and stimulation of the scalene muscles.

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[March 1, 1945]

DISCUSSION ON THE TREATMENT OF ACUTE MENINGITIS

Dr. M. Mitman; *Treatment of meningococcal meningitis.*—For more than thirty years the standard treatment of cerebrospinal meningitis was spinal drainage, serotherapy and skilled nursing. During that period a considerable reduction in case fatality was effected.

From Flexner in 1907 to Sturdee in 1936 a long record of serotherapeutic successes was interleaved with gloomy pages of failures. Reliable figures of the value of serum are difficult to obtain because outbreaks varied in virulence, their natural fatality rate being 40% to 80%. Satisfactory controls in a particular epidemic were usually unobtainable since diagnosed cases were conscientiously treated with serum. Cormack (1913) in Africa, faced with a shortage of serum, was able to make a valuable comparison between 102 cases not treated with serum, of whom 82% died, and 139 more seriously ill patients treated with serum, 54% of whom died. Flexner gave the fatality rate before the introduction of serum as 70% to 80% reduced by serotherapy to 30-9%. Sturdee (1936) found this figure agreed closely with his rate of 27-6% for serum-treated cases. Nevertheless, figures as low as this have been recorded in cases not treated with serum (*vide* Zinsser *et al.*, and Brinton, 1941). Case fatality based on the number of deaths as compared with the number of notifications is unprofitable, indeed deceptive, because notifications were notoriously unsatisfactory and, as late as 1920, instances occurred of deaths exceeding notifications.

The wide variation in the natural case-fatality rate of different epidemics is closely concerned with the type, and more particularly the strain, of the prevalent organism, and is reflected in the number of severe fulminating forms and those with adrenal hemorrhage. Serologically distinct groups have been known since 1909 and experience in the last war emphasized the value of type-specific sera. After a quick typing by a precipitation test on the spinal fluid polyvalent serum was replaced as far as possible by monovalent serum. As Branham (1936) pointed out, the application of this method was limited because specific soluble substances had to be abundant in the cerebrospinal fluid and the patient must not have had serum. Even typing failed to be sufficiently specific and it became clear that a serum prepared from the locally prevalent strain of meningococcus promised best results. A method of management, not often possible, was to cultivate the responsible organism and determine if it was agglutinated by the serum in use; if not, another was sought. In any case, the standardization of antimeningococcal serum was never satisfactory and the value of any particular serum could not be known with certainty. This was very apparent with Ferry's so-called antitoxin, the existence of which was denied by other observers who attributed its value to the usual antibacterial action of sera (2nd Internat. Congr. Microbiol., 1936). Nevertheless, laboratory tests proved that sera were capable of protecting against experimental infection. This uncertainty about the efficacy of sera was reflected in the personal experience of all who had to treat the disease in any numbers. Some cases responded with satisfactory promptitude in two or three days, but the many failures in the most favourable circumstances lent support to the view that the concomitant spinal drainage was the effective therapeutic measure. Introduced by Quinke in 1895, spinal drainage found its logical extension in cisternal and ventricular drainage, and spinal puncture was an essential preliminary to the administration of serum by the route then employed. It was ousted with serum when chemotherapy was established but has been revived with penicillin therapy. But before chemotherapy appeared the intrathecal administration of serum suffered a decline because of the aseptic meningeal reaction it caused. With increasing recognition of the septicæmic nature of the disease intrathecal serum was augmented and, in some instances, entirely displaced by intravenous or intramuscular serum (Herrick, Hoyne, 1935). The theoretical objection to parenteral routes—that serum would not pass the blood-brain barrier—was disproved when it was shown that large molecules could pass through an inflamed choroid plexus. Nevertheless, as late as 1936 Sturdee wrote that "provided the patient comes under treatment at a reasonably early moment, is of suitable age and receives adequate amounts of serum prepared from current strains of meningococci he has a reasonable chance of recovery; also that intrathecal treatment with antimeningococcal serum is the most helpful means of obtaining a good result". With perhaps insistence on some serum being administered parenterally this represented current views.

The sulphonamides transformed the therapeutic scene. Before evaluating them, or indeed any other therapeutic measure, it is essential to enumerate the factors which influence case fatality. This in turn will serve to explain many of the considerable discrepancies between the results of different observers using the same therapeutics. The first factor is the virulence of the prevalent strain of meningococcus reflected in the wide

logical abnormalities in relation to all parts of the following structures must be considered when making a diagnosis and instituting treatment: (1) The clavicle and first rib; (2) the brachial plexus; (3) the cervical vertebrae; (4) the scalene muscles.

It must always be remembered that a combination of abnormalities may be present.

The importance of exact diagnosis in relation to treatment.—If a number of the nerve fibres composing the brachial plexus have undergone Wallerian degeneration, the results of any form of treatment will be disappointing, for the regeneration of peripheral nerves, particularly over long distances, is functionally poor. Howell (1913) reviewed the results of operative treatment in cases with cervical ribs and concluded that, with regard to muscular weakness and atrophy, operation will greatly improve the condition if not too long delayed. It is, therefore, of the utmost importance that an exact diagnosis should be made early in cases of brachial plexus, "irritation" or compression. Careful clinical, radiographic, and electromyographic assessment of each case should be undertaken in order to determine the mechanism giving rise to the symptoms and signs. For instance, in cases of acroparæsthesia associated with pregnancy, the symptoms are probably determined by anatomical changes occurring during the latter half of pregnancy. Respiration becomes more costal in type with consequent elevation of the first rib and is associated with increased activity and perhaps hypertrophy of the scalene muscles which leads to a narrowing of the thoracic outlet. Since the changes responsible for the symptoms are reversible, the treatment is clearly conservative. Similarly in cases with abnormalities of the thoracic outlet in which symptoms and signs have arisen as a result of a change in occupation (leading to a descent of the shoulder girdle) the treatment is conservative in the first instance. In the majority of such cases, the pathological changes are reversible, and cure may be expected to follow the removal of the precipitating cause of the affection. On the other hand, in all cases in which symptoms and signs are progressive despite conservative measures, operation should be undertaken early in order to forestall Wallerian degeneration.

Any operation undertaken should be regarded as exploratory, and should preferably be performed under local anaesthesia. During the course of the operation every attempt should be made, by postural manœuvres and electrical stimulation of the scalenus anticus muscle, to determine both the exact point and mechanism of the compression of the nerves. In some cases division of the scalenus anticus muscle alone will relieve the affection although its primary cause is a cervical rib. On other occasions it may be necessary to remove a segment of the first rib, or to divide a fibrous band occupying the position of a cervical rib.

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SUMMARY

(1) The anatomy of the thoracic outlet has been discussed in relation to "irritation" and compression of nerve trunks. (2) It has been emphasized that the nerves composing the brachial plexus may be subjected to "irritation" or compression at a number of points along their course, and that a number of anatomical and physiological factors may be responsible, either singly or in combination. (3) It is important to establish the precise nature of the anatomical conditions in the establishment of a diagnosis if treatment is to be successful. (4) In cases in which symptoms and signs are progressive, operation should be undertaken as early as possible. Exact confirmation of the diagnosis should be obtained at operation by postural manœuvres and stimulation of the scalene muscles.

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The fourth factor influencing a favourable result is the specific therapy employed. Sulphonamides have reduced enormously the fatality of the disease, practically abolished chronic and relapsing cases, diminished considerably the proportion and severity of complication, and shortened hospitalization to an average of thirty days or so. Thomas attributes the amazing reduction in case-fatality rate from 39% in the last war to 3.5% in this entirely to chemotherapy. I have already referred to rates of 0 to 1% in special groups of Service personnel treated with sulphadiazine. Martin (1942) estimated that sulphonamides saved 10,000 lives in this country in 1939-41 and Stocks (1943) that they saved 2,500 in 1942 alone. When sulphonamides were first introduced it was natural to combine their use with serum and spinal drainage, but reports were soon forthcoming that combined chemo- and serotherapy gave no better results than sulphonamides alone; indeed in some instances the results were worse. Brinton (1941) following Banks (1940, 1941) expressed the view that chemotherapy had rendered treatment with serum as obsolete as routine spinal drainage. He enumerated the disadvantages of the older methods as repeated, often serious, disturbance of the patient for lumbar puncture, the frequency of serum disease, the aseptic meningeal reaction, the costliness of serum, the lack of specificity of the serum and the enormous expenditure of time and labour by the staff. This failure of combined therapy was *a priori* grounds, surprising because the modes of action of serum and sulphonamides are quite different, and a synergic action might be expected. There was some experimental support for this view from work at the Lister Institute, not only on meningococcal infections (Amies, 1940) but with other organisms (Henderson and Gorer). Clinically, however, serum therapy failed as an adjuvant to chemotherapy not only in meningococcal infections (Banks, 1940, 1941; Beeson and Westerman, 1943; Scottish Report, 1944), but also in pneumococcal infections (Plummer *et al.*) and in certain streptococcal diseases (Mitman, 1937). The results of treatment as recorded in two recent large-scale studies, one in England and Wales (Beeson and Westerman, 1943), the other in Scotland (Scottish Report), closely conform. They both include the epidemic of 1940 and in both the sulphonamide most used was sulphapyridine. The English study is of 3,575 case reports submitted to the Ministry of Health by more than 100 hospitals in the two years 1939-41; the Scottish report was founded on 2,223 cases treated in seven selected hospitals. The overall fatality rate in England and Wales was roughly 16% and in Scotland 22%. A group of Scottish cases treated with serum alone had a rate of over 50%. In every age-group combined sero- and chemo-therapy gave significantly worse results than sulphonamides alone. If this difference is true it supports the view of those who attribute the harmful effects of the serum to an aseptic meningeal reaction. Other explanations cannot be ruled out, for in both groups it is possible that those who received combined treatment were more seriously ill than those who received the drug alone, rendering comparison unfair. In both reports the importance of age in the prognosis is brought out, no matter what the form of treatment. Sex had no effect on the fatality. Some unexpected results emerged. One was that earlier hospital treatment did not improve the prognosis: in Scotland the fatality was actually greater among those admitted in the first few days of their illness than in those admitted later in the week. This was probably because the more serious cases came to hospital earlier; it is no justification for delaying treatment. Another surprising finding in Scotland was that sulphanilamide, with the lowest bacteriostatic power, gave better results than sulphapyridine or sulphathiazole. In a more recent study in Chile, Horowitz and Peroni (1944) tried a controlled experiment and found a case-fatality rate of 13.3% with sulphanilamide 10.7% with sulphathiazole and 9.3% with sulphadiazine. Excluding deaths within twenty-four hours, the figures were reduced to 10.7, 6 and 5 but the differences were not statistically significant.

The choice of a suitable sulphonamide has been considerably narrowed recently. There is a definite order of potency as determined by their bacteriostatic power, and this order is the same for meningococci as for other susceptible organisms. It is a clinical factor which determines the choice, viz. the capacity of the drug to cause toxic or other side-effects. Sulphanilamide, and its derivatives resulting from substitution in the amino group, have been displaced by drugs derived from substitution in the amido group—particularly with heterocyclic rings. The chief exception is that sulphanilamide is still used when sulphonamide therapy must be continued in the presence of haematuria caused by one of the other sulphonamides, for sulphanilamide does not cause this side-effect. Sulphapyridine has practically dropped out because of its tendency to cause vomiting. Sulphathiazole is still widely used, but sulphadiazine or one of its methyl substitution products now leads the field. Except for its tendency to cause crystalluria and haematuria, sulphadiazine is less toxic than the others. It is more readily absorbed and more slowly excreted than most of the others: in consequence a higher concentration can be maintained in the blood for a longer period, so that intervals between doses can be lengthened to six,

variations in fatality rates between one epidemic and another, and between endemic and epidemic cases. Whilst there is a relationship between Group I organisms (Types I and III of Gordon) and epidemics, and a tendency for Group II organisms to affect those in the dangerous age-group, viz. infancy and old age, virulence is, I think, more concerned with an epidemic strain than with a particular type. The second factor, equally important, is the host factor. Immunity to meningococcal infection and ability to withstand a clinical infection are closely related to age. Lassen (1942) makes the point that meningitis under endemic conditions is preponderantly a disease of infants and young children; under epidemic conditions it is widely distributed over all age-groups up to 30 years, and is also more common in the older age-groups; in war it is a serious military disease. No matter what the form of treatment the results are always best in the young adult group and most serious at the extremes of life. Many of the remarkable results among Service personnel in this country and the U.S. have been achieved in the most favourable age-groups; for example, Hill and Lever (1943) report no deaths in 68 consecutive cases treated with sulphadiazine; Daniels *et al.* (1943) reports a case fatality of 1¼% among 80 cases of meningitis, no fatal cases among 32 patients with meningococæmia, giving an overall rate of 0.89% in 112 soldiers treated with sulphadiazine during an epidemic. Taranto (1943) using the same drug on 100 consecutive cases in a U.S. naval camp had a fatality rate of 1%. By contrast, infants under 1 treated in Scotland between 1936 and 1941, chiefly with sulphapyridine, had a case-fatality rate of 28.3%; in patients over 35 years of age it was 35.4%; and in the most favourable age-group it was only 2.6%. Compare this with 1907-8, one of the peak periods of the last forty years, when the rate was 90.4% in infants under 1 year and 74% in young adults (Scottish report).

The third factor influencing a favourable result in meningococcal infections is the organization for early diagnosis and prompt, efficient treatment. In a report on a severe epidemic in the U.S. 4th Service Command (Thomas, 1943) there were 1,935 cases from December 1942 to January 1943, with a case-fatality rate of 3.3%. When this figure was analysed it was found that, for the first month, the case-fatality rate was as high as 12.8%; as the organization for prompt diagnosis began to operate the figure fell, the lowest being 1.5%. The measures introduced included instruction and stimulation of interest in the disease among the inexperienced medical and nursing officers, who thereafter were constantly on the look-out for cases. Patients were transferred to the care of medical officers of the contagious diseases section who had experience of the disease. Before the reorganization some patients were admitted in the evening and seen by the officer of the day who, in many instances, was surgically inclined and not familiar with the disease in its septicæmic phase. Deaths occurred in hospital before a diagnosis was made. The vital significance of premeningeal diagnosis lies in the amazing speed with which early administration of sulphonamides brings the septicæmia to an end. That this stage of the disease was readily responsive to specific therapy was evident from Applebaum's (1937) paper on chronic meningococcal septicæmia which appeared before sulphonamides were generally available. He found the condition responded promptly to intravenous antimeningococcal serum, moderate, but not massive, doses sufficing. The promptness with which the diagnosis of meningococcal infection is made in an epidemic is indicated by the percentage diagnosed in the septicæmic stage. Figures from the U.S. are impressive. Daniels *et al.* (1943) record that during an epidemic when the index of suspicion was high, the figure was 35%; other figures are 28% (Thomas, 1943) and 19% (Hill and Lever, 1943). All are agreed that it is possible to diagnose early meningococcal septicæmia on clinical grounds alone in a high proportion of cases. All degrees of severity and duration of septicæmia occur from the fulminating to the chronic, now well known from the works of Solomon (1902), Rolleston (1919), Applebaum (1937), Heinle (1939), Stott and Copeman (1940), Dickson *et al.* (1941), Copeman (1942) and Morison (1943). Hill and Lever give the four cardinal symptoms of the acute form as headache, vomiting, chill and rash. Daniels *et al.* regard the presence of a rash as essential for the diagnosis and it was therefore present in 100% of their cases although frequently repeated search was sometimes necessary. Petchial, macular, papular, nodular and pleomorphic eruptions of varying degrees of profusion were recorded. Upper respiratory tract infection (the usual mode of onset) was present in 78%, headache (not the meningitic type) in 78%, nausea or vomiting in 59% (a highly suggestive figure in patients suffering from what might be regarded as an ordinary upper respiratory tract infection), chill in 47% and pains in joints in 37%. Pyrexia, polymorphonuclear leucocytosis and herpes simplex were common. All the cases recovered with sulphadiazine, the macular-papular element of the rash disappearing within twelve to eighteen hours: this response to sulphonamide therapy was regarded as diagnostic.

or comatose and change to 1.5 grammes of oral sulphadiazine four-hourly two days after the temperature recedes. Daniels *et al.* in their big-dose series gave 0.1 gramme per kilo body-weight intravenously as the loading dose which is equivalent to 6 grammes in an ordinary person, followed by half this dose eight-hourly subcutaneously until the patient could take by mouth, when 1 to 2 grammes was given four-hourly until the temperature was normal for 5 to 7 days. In the second half of their series they practically halved these doses with the beneficial results I have already mentioned. Thomas gave a loading dose of 5 to 8 grammes to his severely ill patients but in milder cases his doses were smaller than those I have advocated. Little use appears to have been made in America of administration of the drug by nasal or oesophageal tube as an alternative to the intravenous route for the comatose or stuporose.

Sulphonamide therapy alone usually suffices in about 95% of cases. The remainder include fulminating cases and those showing evidence of circulatory collapse, who require adjuvant therapy. Banks and McCartney maintain that this group includes those with encephalitic syndromes, pure adrenal syndromes, and mixed adrenal and encephalitic syndromes. They recommend that the term Waterhouse-Friderichsen syndrome should be dropped because it includes more than one of the above types. Certainly there is no historical justification for its retention. Banks and McCartney maintain that in the pure adrenal syndrome the mental condition remains clear to the end whereas in the graver, mixed syndrome there is early coma which persists or deepens.

The classical description of the adrenal syndrome is of an illness of apoplectic onset in a previously well infant under 2 years of age: early circulatory collapse, a hæmorrhagic rash and death within twenty-four hours is the course; post-mortem shows massive bilateral adrenal hæmorrhages (Waterhouse, 1911; Friderichsen, 1918; Grace *et al.*, 1940; Harries, 1940, 1942; Murphy, 1940; Lindsay *et al.*, 1941; Morison, 1943). The syndrome is not limited to infants and although the cause is nearly always meningococcal, it is not invariably so. I recollect being called to see an A.T.S. suspected to be suffering from smallpox. The previous night she had been taken ill at a dance, had vomited, and had been regarded as a little intoxicated; so she was, but not by alcohol. Next morning she was stuporose, pyrexial and had an extensive hæmorrhagic rash. She died within twenty-four hours. Post-mortem showed hæmorrhages in all organs, very marked in the suprarenals. Although the provisional diagnosis in life had been cerebrospinal fever, pneumococci were cultured from the blood and fauces, and paired cocci were seen in suprarenal smears.

Milder degrees of circulatory collapse, from which recovery occurs, are seen in severe cases. On the theory that they are due to temporary adrenal failure, substitution therapy is used. Morison (1943) considers the condition akin to shock; treatment, he suggests, should be directed to the disturbed hydrodynamics and plasma transfusions given in all fulminating infections; adrenal substitution therapy he regards as secondary. Both adrenal cortical extract and desoxycorticosterone acetate have been used. Hill and Lever recommend the hypodermic injection of 2 c.c. of the extract several times in the first twenty-four hours and twelve-hourly thereafter until the blood-pressure is restored. Thomas gives 30 to 50 c.c. followed by smaller doses at frequent intervals. He also advocates adrenaline by continuous intravenous drip. Murphy recommends 5 mg. of desoxycorticosterone acetate intramuscularly six-hourly during the acute stage. For the sodium depletion and water loss, intravenous administration of 1,000 c.c. of an isotonic solution of sodium chloride, or a sixth molar solution of sodium lactate may be given at the same time as the intravenous sulphonamides. The hypoglycemia resulting from disturbance of the glucose metabolism is overcome by the addition of 5% glucose and the intravenous saline solution. It is suggested by Murphy that if bromides are indicated for sedation, they should be given as the sodium salt because of the presence of a high blood-potassium level in adrenal lesions. The prompt and efficient treatment of severe and fulminating cases therefore entails considerable skilled medical and nursing care which I summarize as follows:

(1) A diagnostic lumbar puncture must be performed at once for cytological, biochemical and bacteriological examination of the fluid.

(2) A blood culture, a white blood-count and a differential count must be carried out.

(3) If the condition is clinically a meningococcal septicæmia or meningitis, therapy must begin immediately, regardless of the appearance of the fluid or the laboratory report. The diagnosis of meningitis is of course confirmed by a turbid fluid or a positive smear.

(4) For the treatment of the infection chemotherapy in the form of sulphadiazine given along the lines indicated is the method of choice and must be instituted immediately the diagnosis is suspected. It should be controlled by daily measurements of the

even eight, hours, a valuable property when treating seriously ill patients urgently in need of sleep. The concentration of the drug in the cerebrospinal is 50%—80% of that in the blood, compared with 15%—40% in the case of sulphathiazole. But routine estimations of sulphonamide concentration even in blood are not always practicable and estimation of levels in the cerebrospinal fluid involve lumbar punctures. The Americans attach great importance to controlling therapy by routine estimation of sulphonamide levels in the blood. The optimum concentration for sulphadiazine is not known but 10 to 15 mg.% is usually regarded as necessary for severe infections and anything below 8 mg.% as inadequate. Although there is some correlation between blood levels and therapeutic success it is not high, the effectiveness of therapy being best judged from the clinical response. There is, however, a place for estimation of blood levels in cases failing to respond, for an unusually low concentration due to some anomaly of absorption, excretion, acetylation or metabolism, or to excessive fluid intake, spells failure. As the solubility of sulphadiazine in urine is low, particularly when the urine is acid and concentrated, as it is in severe pyrexial conditions, an essential step in management is the avoidance of crystalluria. The aim should be to secure the daily excretion of 40 to 50 oz. (1,200 to 1,500 c.c.) of an alkaline urine (pH > 7.5) with a specific gravity below 1014. An intake of about 5 pints (3,000 c.c.) of fluid is required and sodium bicarbonate, citrate or lactate prescribed to effect the alkalization of the urine, which is not always possible. I use the mist. sod. cit. of the N.W.F. half an ounce or more with each oral dose of sulphadiazine. I am, however, opposed to excessive fluid intake; there is a tendency for a vicious circle to be set up: excessive doses of sulphonamides are given, particularly loading intravenous doses; excessive fluid is administered to minimize crystalluria; the sulphonamide is washed out of the circulation and the net result is the same as if a smaller dose had been given with less fluid, whilst the danger of urinary complications has been increased.

The comparative value of high and low dosage of sulphadiazine has been debated frequently. Daniels *et al.* (1943) found that patients treated with lower doses fared better than those given higher doses, although it must be mentioned that the disease was declining in severity when the lower dosage was employed. The important difference was in the incidence of renal complications. In the high dosage group 15% had gross hæmaturia and 6% anuria, whereas in the lower dosage group there were no such cases. In both the English and Scottish surveys it was noted that those who received doses as high as, or higher than, Banks recommended fared no better than those who received moderate doses. It should be remembered that in suitable cases even a single dose of sulphonamide may have an appreciable influence probably by breaking the vicious circle which determines all overt infections. The effect of a single dose on the bacteriological findings is significant. Daniels *et al.* obtained bacteriological confirmation of their diagnoses from blood or spinal fluid in 78% of cases; in a group provided with special laboratory facilities the figure was increased to 95%; but the organism was never grown from the blood or fluid of a single patient who had been previously treated with a sulphonamide despite the addition of an antisulphonamide to the culture media. From the work of Somers, and Bryant and Fairman (1939) in the Sudan and from observations in their own clinic, Meads *et al.* (1944) expect a single dose of 2 to 4 grammes of sulphonamide, given when the diagnosis is suspected, to be sufficient to produce beneficial results in favourable cases; and that in estimating the value of penicillin in the treatment of meningitis, it must be certain that not a single dose of sulphonamide has been given. They were commenting on Rosenberg and Arling's excellent results—75 recoveries out of 76 cases treated with penicillin—which they were unable to reproduce. I am therefore in favour of moderate dosage.

For the average case of cerebrospinal fever an adequate amount consists of 9 grammes daily until the temperature is normal, i.e. for about three days, reduced by a third to 6 grammes daily for another two or three days, and completing the course by another reduction to 3 grammes daily for another two or three days, the total dosage being about 40 to 50 grammes extending over a week. Milder cases require only two-thirds of this dosage. For the first period the doses should be given four-hourly; thereafter if progress is satisfactory the intervals may be increased to six hours. The initial or loading dose if given by mouth or nasal tube should be heavy, namely 4 grammes; if given intravenously it should be two grammes only as flooding of the circulation with a massive intravenous dose particularly predisposes to hæmaturia.

I am bound to point out that these doses are much smaller than those advocated by others. Hill and Lever give all the sulphonamides in the first twenty-four hours by the intravenous route in three doses at eight-hour intervals. The first dose is 5 grammes and the next two 2.5 grammes. They repeat intravenous medication if the patient is still stuporose

and not more than a few degenerate organisms seen on the direct film. The cell count usually rises, and if the C.S.F. has thickened appreciably a third puncture should be done twelve hours later to make sure of detecting any incipient block. Thereafter daily injections are usually sufficient, but must be continued for at least five days. The intramuscular penicillin can usually be stopped after four days, but though the sulphadiazine can be cut down to 1 gramme every four hours, it should be given for at least a week in order to cover the period of withdrawal of the intrathecal penicillin.

During the first twenty-four hours the disappearance of organisms from the C.S.F. is usually the only sign of improvement; this period is one of great anxiety and the importance of the general nursing care, adequate sedation and the maintenance of a good fluid intake cannot be exaggerated.

This scheme of treatment is not offered as a rigid routine, but rather represents the safe minimum in an uncomplicated case and will suffice in perhaps one-half of cases.

The principles of treatment and their practical application.—(1) Early institution of treatment. (2) Free access of adequate amounts of penicillin to all parts of the cerebrospinal pathways. (3) Maintenance of an adequate concentration of penicillin in the C.S.F. for a sufficient length of time. (4) Treatment of the primary focus.

(1) *Early institution of treatment.*—It is neglect of this principle that causes the greatest number of failures. In addition to our fully treated cases we have had three in which the patient was moribund on admission to hospital and died within the next few hours.

Delay in treatment is usually due to delay in diagnosis. Three types of onset are seen: the fulminating, the acute, and the insidious. In the fulminating type the onset resembles that of subarachnoid hæmorrhage and the diagnosis is only made by lumbar puncture. In the insidious type the signs of meningitis are often masked by those of the primary infection. The acute type is the commonest; clinical diagnosis is seldom difficult, but early identification of the organism is essential.

When no facilities for immediate bacteriological examination of the C.S.F. exist, the differentiation must be attempted on clinical grounds. Meningococcal meningitis should be suspected when there is no evidence of a primary focus of infection; while the presence of a primary focus, situated most commonly in the ears or nasal sinuses, is the rule in pneumococcal and streptococcal meningitis.

Treatment with full doses of sulphonamides should be begun immediately, but where there is no evidence of a primary focus penicillin should probably be withheld pending bacteriological examination, as it is seldom needed in the treatment of meningococcal meningitis. Even when a primary focus is found, penicillin should probably be withheld until a film of the C.S.F. has been examined in all except the fulminating cases, because of the frequency with which streptococcal meningitis is complicated by an intracranial abscess. This demands radical modifications in treatment, otherwise death may be precipitated by lumbar puncture.

In fulminating cases in which a primary focus of infection is present penicillin should probably be given at the time of the initial lumbar puncture, since sulphonamides alone seem useless and if untreated the disease may run its full course within twenty-four hours.

(2) *Free access of penicillin to all parts of the cerebrospinal pathways.*—The methods of treatment are conditioned by the fact that the meninges are relatively impermeable to penicillin. Effective concentration in the C.S.F. can therefore only be achieved by direct intrathecal injection, using either the lumbar, cisternal, or ventricular route. Free circulation throughout the subarachnoid space and the ventricular system is essential.

The lumbar route is the simplest and is effective provided the cerebrospinal pathways are patent. Occasionally these may be blocked by a complicating intracranial abscess, and though this is exceptional (in striking contrast to the frequency of abscess formation in streptococcal meningitis), the development of focal signs is usually an indication for a ventricular tap.

More commonly, a subarachnoid block may develop from the deposition of fibrinous pus. This may occur in the first few days of the disease and should be suspected if the flow of C.S.F. on lumbar puncture becomes sluggish. This alteration in the flow, with difficulty in obtaining more than a few drops of C.S.F., is the earliest sign of impending block and an absolute indication of cisternal or ventricular injection.

(3) *Maintenance of an adequate concentration of penicillin in the C.S.F. for a sufficient length of time.*—Intrathecal treatment should be given for a minimum of five days, and only withheld when the patient is obviously approaching convalescence. Relapses are common: 3 of our fatal cases died in relapse, and a further 7 had one or more relapses before they finally recovered. To allow the concentration of penicillin in the C.S.F. to fall prematurely is to invite relapse. The penicillin content of all specimens of C.S.F.

intake and output of fluids and by daily urinalysis with special reference to specific gravity, alkalinity and the presence of crystals. If facilities are readily available periodic estimation of blood levels of sulphadiazine are a useful check.

(5) For the treatment of circulatory collapse plasma transfusions are indicated to correct the disturbed hydrodynamics, adrenal substitution therapy for the adrenal failure, and control of the electrolyte balance and carbohydrate metabolism along the lines indicated.

Blood pressures should be taken daily for at least the first three days.

(6) Although I have not mentioned routine nursing measures they are still an important part of the treatment of meningitis. Sedation, adequate nourishment, care of the skin and a watch on the bladder are first considerations.

(7) I consider a second lumbar puncture prior to discharge a desirable release measure but I am now less certain of the need for release nasopharyngeal swabs.

The place of penicillin in the treatment of meningococcal infection is still uncertain. A little while ago I should have said that with its absence of toxicity it was likely to displace sulphonamides entirely. But recent reports (Meads *et al.*) indicate that at present its position may be adjuvant and that sulphonamides are still the drug of choice.

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Dr. Honor Smith: *The chemotherapy of pneumococcal meningitis* [Summary].—Up to the present time we have had 29 fully treated cases of pneumococcal meningitis with 4 deaths from meningitis and 1 from unrelated causes. The first 16 cases were treated with penicillin alone. In most of these cases sulphonamides had previously been given, and it was realized that these drugs could frequently prevent or delay clinical deterioration, though seldom effect a complete cure. Accordingly, in our last 13 cases both sulphonamides and penicillin were used and all the patients recovered from their meningitis.

Routine of treatment.—As soon as a diagnosis of pneumococcal meningitis is made an injection of 8,000 to 20,000 Oxford units of penicillin is given by lumbar puncture. The exact dose depends on the age and size of the patient and on the severity of the infection as judged by the length of history and the patient's general condition. Systemic treatment is begun by intramuscular injections of penicillin and 120,000 units given every twenty-four hours. Sulphadiazine is given by mouth or nasal tube in doses of 2 grammes every four hours following an initial dose of 4 grammes. This is given, with the usual precautions against renal block, to supplement the action of the intrathecal penicillin, while we only depend on the intramuscular penicillin to control the primary infection, since in this dose none of it penetrates the theca. Early next day the lumbar injection is repeated. The C.S.F. should now be sterile

Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[May 1, 1945]

The Consideration of Functional Disabilities in Orthopædics

By Major W. E. TUCKER, R.A.M.C.

In every branch of medicine the functional disability of each case should be considered by the medical officer concerned.

It is my purpose to give a short survey from the functional disability aspect of 529 orthopædic cases which have passed through a Military Hospital and Convalescent Home over a period of ten months.

This investigation was an endeavour to assess and treat the functional disability concurrently with the orthopædic condition in a group of soldiers examined in a Military Hospital. These represent a cross-section of cases drawn from an Infantry Training Centre, paratroopers, wounded and sick from overseas and various holding depots.

The functional element was not severe enough to refer them to a psychiatrist except in a few cases and, in fact, it was thought to be more in their interest to treat them by direct methods than to allow them to consider themselves ill enough to be sent to a psychiatrist. The soldier to whom these more direct methods are applied will often confide in one quickly and in a short time it is possible to find out what is fundamentally at fault.

An endeavour was made to estimate the percentage of functional disability under the following headings: (1) Domestic worries; (2) Anxiety; (3) Hysteria; (4) Malingering; (5) Unsuitable employment.

The estimations were made in consultation with the matron and a physiotherapist, who also had the patients under constant observation in the convalescent home.

TABLE I.—SUMMARY OF CASES

Total receiving treatment	529
Before treatment	{ No functional disability	166
	{ Functional disability	363
After treatment	{ No functional disability	153
	{ Decreased functional disability	158
	{ No improvement	52
Referred to psychiatrist	7

Comment.—In this series, as a rough estimate, 2 out of 3 cases showed some degree of functional disability. Of the 210 cases not completely cured of their functional disability 158 showed some improvement.

In these cases under review showing functional disability some pathological condition was or had been present. This pathological state, traumatic or otherwise, was made the basis for treatment, which consisted of careful explanation, encouragement combined with operation or physiotherapy and exercises.

Minor pathological conditions such as would give rise to painful feet or low back pain cannot be permanently improved at a convalescent home, depot or physical development centre unless a full explanation of the part the muscles play in maintaining posture is given, and then the correct use of the muscles comes into the conscious mind of the soldier, so that by constant practice the action becomes a habit.

Factors producing a functional disability June 1944 to March 1945:—

Domestic worries.—Common everyday worries.

Anxiety.—If the patient develops some orthopædic condition such as early osteoarthritis while serving in the Army, an anxiety state as to his future ability to join in the struggle for existence after the war often becomes superimposed on his disability. A great deal can be done for this man by explanation and getting him to face up to his disability as well as by giving him careful instructions as to how to keep the condition under control.

While in Germany one noticed that patients were constantly considering how much disability pension they would receive for their wounds. If these were of a trivial

should be estimated and the intervals between injections adjusted so that an effective concentration is present throughout the whole course of intrathecal treatment.

(4) *Treatment of the primary focus.*—We rely on the intramuscular injections of penicillin to control the primary infection. This has proved so satisfactory that even in cases secondary to a mastoiditis we have never found it necessary to operate during the acute stage of the meningitis.

Dangers of intrathecal treatment with penicillin.—Some preparations of penicillin are extremely irritating and capable in themselves of causing a brisk sterile meningitis. There is also considerable risk of introducing a secondary infection into the theca, either through faulty lumbar puncture technique or from contamination of the penicillin solution. A full aseptic technique must be used for all intrathecal injections, and the penicillin solution should be freshly sterilized by Seitz filtration and put up in small quantities so that only a limited number of injections can be given from any one container.

Results.—Since March 1943 we have treated in all 32 cases with 8 deaths. 1 of these was due to unrelated causes (fat embolism). 3 were moribund when treatment was begun. 2 died from a complicating intracranial abscess. In the remaining 2 the initial response was good, but subarachnoid block developed with subsequent relapse and death.

In 2 of the surviving cases recovery was incomplete. 1 of these was a child who had developed a severe posterior-basis syndrome before treatment with penicillin was begun; the other an elderly woman who had been a chronic invalid for over two years before contracting meningitis.

In no other case were any after-effects detected other than a temporary tendency to undue fatigue. Both mental and physical recovery was complete.

Dr. E. S. Duthie: *The chemotherapy of pneumococcal meningitis [Summary].*—In the treatment of pneumococcal meningitis by the intrathecal administration of penicillin, we have used whenever possible preparations of about 500–600 units/mg., i.e. about 30% pure. This was made up to 2,000 units/c.c. in pyrogen-free saline, Seitz filtered and stored in 8 c.c. amounts in the cold until required. The usual dose of this solution lay between five and ten thousand units. Strict asepsis using a non-touch technique is essential in its administration. Introduction of *Ps. pyocyaneus* is the chief danger, and the sterility of the skin and of the infiltrating solutions should be beyond question.

Pneumococci are almost uniformly sensitive to 1/40 unit per c.c., streptococci rarely require more, while about 10 to 20% of staphylococcal strains produce penicillinase and are relatively resistant. We have found no alteration in the sensitivity of the pneumococci encountered during treatment, which in some cases extended over several months. Large doses of penicillin given intramuscularly may pass the blood-brain barrier in very small amounts, if the meninges are inflamed. The level is, however, too low for efficient therapy.

Penicillin injected intrathecally either by the lumbar or by the ventricular routes is rapidly dispersed throughout the cerebrospinal pathways, and will reach an efficient level everywhere in less than two hours, provided there is no blockage present. In the majority of cases between 0.1 and 1.0 units/c.c. are present at the end of twenty-four hours, but some individuals lose penicillin very rapidly and in one case in the series there was none present in the C.S.F. six hours after the injection of between 5,000 and 10,000 units. In this case the unusually rapid loss was associated with a subdural hydroma following fracture. The rate of penicillin loss diminished and became normal when the hydroma cavity healed after operation. Thus constant penicillin estimations are essential for efficient therapy in order that any unusually rapid loss of penicillin from the C.S.F. may be detected.

Penicillin has a killing action only on the growing bacterial cell. Resting bacteria are likely to be present in dead tissue such as abscesses, and will be unaffected by the drug. Cure may result either through surgical removal of the focus, or by maintaining the penicillin treatment until the dead tissue has been absorbed. Sulphonamides do not interfere with the killing action of penicillin. They should be used to supplement it, since they exert a synergic action, and it is often difficult to maintain an efficient penicillin level over the whole period between injections.

Pure penicillin is probably non-toxic in large amounts, but many commercial samples contain impurities which may set up an aseptic meningitis. Specimens smelling of amyl acetate and those causing skin reactions or pain on injection, should not be used intrathecally. We therefore advocate using only the purest preparations available, which may be checked by giving a first injection of 2,000 to 4,000 units intrathecally. If there are no toxic reactions as shown by increase in the signs of meningeal irritation, impairment of the ankle-jerks or alterations in the pulse or respiration rate, a second injection of double the amount may be given six to eight hours later. A reaction-free batch of penicillin should be put aside for future intrathecal injections only. One case in our series, a child of 17 months, had 391,000 units intrathecally in 50 lumbar injections over fifty days, without any toxic reactions whatever. Since nowadays every precaution is taken by the manufacturer to prevent contamination of the penicillin marketed, Seitz filtration may be unnecessary provided strict asepsis is used in making it up.

TABLE III.—WAR WOUNDS.

No functional disability Case no.	Functional disability per cent.											
	Before treatment							After treatment				
No.	DW	A	H	M	UE	Total	DW	A	H	M	UE	Total
2	93	30	50	—	—	—	20	20	—	—	—	40
15	167	20	10	25	25	—	10	10	10	10	—	40
24	44	30	10	20	—	—	10	10	10	—	—	30
26	239	10	20	10	20	—	10	10	—	10	—	30
28	101	20	10	10	10	—	10	5	5	—	—	20
49	110	20	10	10	10	—	—	10	—	—	—	10
513	118	30	20	—	—	—	30	10	—	—	—	40
63	142	20	10	10	10	—	20	5	5	—	—	30
82	299	20	10	20	—	—	20	5	5	—	—	30
83	464	—	20	20	10	—	—	5	10	5	—	20
96	25	—	20	20	—	—	—	20	20	—	—	40+
97	120	—	20	10	10	—	—	10	10	10	—	30
125	139	—	20	20	—	—	—	5	5	—	—	10
137	191	20	10	—	10	—	20	10	—	10	—	40+
194	226	20	10	10	—	—	—	10	10	—	—	20
212	346	10	20	10	—	—	5	—	5	—	—	10
213	427	—	20	10	10	—	—	20	10	10	—	40+
237	143	—	10	20	—	—	—	—	—	—	—	0
264	156	20	10	—	—	—	20	10	—	—	—	30+
269	290	10	20	—	—	—	10	—	—	—	—	10
270	331	10	10	10	—	—	10	5	5	—	—	20
307	340	—	10	10	10	—	—	5	—	5	—	10
316	375	10	10	10	—	—	—	5	5	—	—	10
389	415	10	20	—	—	—	—	10	—	—	—	10
404	426	—	20	10	—	—	—	10	—	—	—	10
390	498	—	20	10	—	—	—	10	10	—	—	20
355	48	—	—	20	—	—	—	—	10	—	—	10
445	57	—	20	—	—	—	—	10	—	—	—	10
468	95	20	—	—	—	—	20	20	—	—	—	20+
477	98	—	20	—	—	—	—	10	—	—	—	10
485	183	—	20	—	—	—	—	10	—	—	—	10
483	184	—	20	—	—	—	—	10	—	—	—	10
484	221	—	20	—	—	—	—	10	—	—	—	10
481	257	—	10	10	—	—	—	—	—	—	—	0
494	263	—	20	—	—	—	—	10	—	—	—	10
503	293	—	20	—	—	—	—	—	—	—	—	0
405	297	—	20	—	—	—	—	10	—	—	—	10
	323	—	10	10	—	—	—	10	10	—	—	20+
	332	10	10	—	—	—	10	—	—	—	—	10
	339	—	10	10	—	—	—	5	5	—	—	10
	343	—	10	10	—	—	—	5	5	—	—	10
	379	—	20	—	—	—	—	—	—	—	—	0
	399	10	10	—	—	—	5	5	—	—	—	10
	416	—	20	—	—	—	—	10	—	—	—	10
	195	10	—	—	—	—	—	—	—	—	—	0
	205	—	10	—	—	—	—	—	—	—	—	0
	228	—	10	—	—	—	—	—	—	—	—	0
	246	—	10	—	—	—	—	—	—	—	—	0
	276	—	10	—	—	—	—	—	—	—	—	0
	304	—	10	—	—	—	—	—	—	—	—	0
	364	—	10	—	—	—	—	10	—	—	—	10+
	376	—	10	—	—	—	—	10	—	—	—	10+
	386	—	10	—	—	—	—	—	—	—	—	0
	439	—	10	—	—	—	—	5	—	—	—	5
	441	—	10	—	—	—	—	—	—	—	—	0
	473	—	10	—	—	—	10	10	—	—	—	10+

+ Indicates cases showing no improvement.

(2) Explanation of disability and reason for anxiety state. Attempts were made to get the patient to appreciate his disability and indicate how he might face up to it.

(3) Constant encouragement—realization of the difference between symptoms which are physiological and those which are pathological. By this is meant appreciation that excessive muscular action often produces stiffness and pain and that these can easily be corrected by graduated training at the same time as carrying out simple remedies such as contrast baths, massage and manipulation of affected parts by the patient himself.

(4) Endeavour to help in domestic worries and placing the soldier in the right category and employment. Help in this was received from the Padre, unit officer, and, in some cases, the welfare officer. Suggestion plays the most important part in the treatment.

To sum up, I regard it as one of the most important duties of the orthopaedic surgeon to consider, assess, and treat the functional disability aspect of his cases and, in so doing, to check anxiety and hysterical states which so often starting from minor orthopaedic conditions produce relatively severe functional disability.

I wish to record my thanks to Colonel Ellcombe, A.D.M.S., and Lieut.-Colonel Anderson, O.B.E., our C.O., for granting facilities and permission to give this paper.

A Modified Smith-Petersen Nail for Fractures of the Neck of the Femur.—W. H. GERVIS, F.R.C.S.

The ordinary Watson-Jones type of nail has the disadvantage that it may slip out with consequent re-displacement of the fracture (fig. 1).

nature, or the patient was obviously unduly anxious, he was told candidly how much it was considered he would receive in pension. It was a great shock at first to the patient who considered he would receive a substantial benefit for the rest of his life to be informed that he would be lucky to be awarded any pension at all. On the other hand, it made him realize that he was not so badly incapacitated and that it was in his own interests to rehabilitate himself as quickly as possible.

In some cases, especially those wounded by enemy action, anxiety that they would be sent out again before they were absolutely fit played a more important role than the actual fear of going into action again. These soldiers know that modern warfare requires a sound body and after being wounded they wish to feel completely fit to withstand the strain which they expect to encounter.

Hysterical manifestations usually occurred as a muscular inco-ordination.

Malingering appeared to be uncommon but cases can be classified as borderline in which the patient will not apply sufficient effort or conscientiously carry out treatment prescribed.

Unsuitable employment leads to unhappiness and the fear of return to such employment is a factor in producing functional disability and a failure in ultimate efficiency. Types in which the foregoing may be found are:

(1) Those cases of fracture of the long bones which, as the war in Europe is reaching its termination, hope for their discharge.

(2) Those cases with a slight disability who hope by continually being off work to be placed in a low enough category to be eventually discharged from the Army.

(3) Wounded men being evacuated to the hospitals nearest their homes sometimes have to pass through many hospitals with the result that treatment is disjointed and therefore insufficient.

(4) Those who observe their friends in civilian life having a good time and therefore feel that they have done their bit.

(5) Those who have good jobs awaiting them in civilian life.

TABLE II.—ANALYSIS OF CASES

Type of case	Total	Before treatment		After treatment		
		No funct. disab.	Funct. disab.	No funct. disab.	Decreased funct. disab.	No improvement
War wounds ...	93	37	56	12	35	9
Knee conditions ...	143	46	97	46	33	18
Simple fractures ...	175	58	117	65	43	9
Compound fractures ...	15	5	10	3	5	2
Rheumatism ...	8	1	7	1	4	2
Foot conditions ...	24	4	20	3	12	5
Low back pains ...	5	0	5	1	4	0
Sprains of joints ...	32	8	24	12	9	3
Miscellaneous ...	21	6	15	4	9	2
Finger amputations ...	9	1	8	3	3	2
Nerve lesions ...	4	0	4	3	1	0

Type of case	Before treatment						After treatment					
	Functional disability—average per cent.						Average per cent.					
	DW	A	H	M	UE	Total%	DW	A	H	M.	UE	Total%
War wounds ...	6.4	14.1	6	2.2	0	28.7	4	6.4	3	1	0	14.4
Knee conditions ...	2.2	11.4	4	3	0.5	21.1	1.6	4.2	2.1	1.6	0	9.5
Simple fractures ...	3	12	6	3.1	0.5	24.6	2	3.2	2	1.3	0	8.5
Compound fractures ...	10.5	9	5	5	1	30.5	7.5	4.5	3	3	0.5	18.5
Rheumatism ...	7	15.7	7	1.4	1.4	32.5	5.7	9.3	3.6	1.4	0	20
Foot conditions ...	3.5	17.5	6.5	4.5	1.5	33.5	2.5	11	4.7	3	1.5	29.7
Low back pains ...	4	16	8	2	4	34	2	10	2	0	0	14
Sprains of joints ...	5	12.5	4.7	2.5	0.4	25.1	1.6	3.7	2	1.2	0	8.5
Miscellany ...	6	12.6	6.6	3.3	0.6	29.1	4.6	6	3.6	1.6	0	15.8
Finger amputations ...	9	14	6.2	2.5	0	31.7	7.5	5	3.1	2	0	18.6
Nerve lesions ...	0	12.5	2.5	0	0	15	0	2.5	0	0	0	2.5

Key to abbreviations, Tables II and III:—

DW=Domestic worries. A=Anxiety. H=Hysteria. M=Malingering.

UE=Unsuitable employment in the Army.

Comment.—The functional disability factor was greatest in patients with low back pain, foot conditions and rheumatism, as would be expected.

The further tables analysed were: Knee conditions; simple fractures; compound fractures; rheumatism; foot conditions; low back pain; sprains of joints; miscellaneous; finger amputations; nerve lesions. These tables cannot be printed here owing to lack of space.

The methods of treatment included: (1) The ordinary orthopaedic measures, at the same time keeping the psychological aspect in mind. Naturally, these measures were directed to curing the pathological condition and included operations, physical treatment, exercises and the right use of muscles.

TABLE III.—WAR WOUNDS.

No functional disability Case no.	Functional disability per cent.											
	Before treatment							After treatment				
No.	DW	A	H	M	UE	Total	DW	A	H	M	UE	Total
2	93	30	50	—	—	80	20	20	—	—	—	40
15	187	20	10	25	—	80	10	10	10	10	—	40
24	44	30	10	20	—	60	10	10	10	—	—	30
26	239	10	20	10	20	60	10	10	—	10	—	30
28	101	20	10	10	10	50	10	5	5	—	—	20
49	110	20	10	10	10	50	—	10	—	—	—	10
513	118	30	20	—	—	50	30	10	—	—	—	40
63	142	20	10	10	10	50	20	5	5	—	—	30
82	299	20	10	20	—	50	20	5	5	—	—	30
83	464	—	20	20	10	50	—	5	10	5	—	20
96	25	—	20	20	—	40	—	20	20	—	—	40+
97	120	—	20	10	10	40	—	10	10	10	—	30
125	139	—	20	20	—	40	—	5	5	—	—	10
137	191	20	10	—	10	40	20	10	—	10	—	40+
194	226	20	10	10	—	40	—	10	10	—	—	20
212	346	10	20	10	—	40	5	—	5	—	—	10
213	427	—	20	10	10	40	—	20	10	10	—	40+
237	143	—	10	20	—	30	—	—	—	—	—	0
264	156	20	10	—	—	30	20	10	—	—	—	30+
269	290	10	20	—	—	30	10	—	—	—	—	10
270	331	10	10	10	—	30	10	5	5	—	—	20
307	340	—	10	10	10	30	—	5	—	5	—	10
316	375	10	10	10	—	30	—	5	5	—	—	10
389	415	10	20	—	—	30	—	10	—	—	—	10
404	426	—	20	10	—	30	—	10	—	—	—	10
390	498	—	20	10	—	30	—	10	10	—	—	20
355	48	—	20	—	—	20	—	—	10	—	—	10
445	57	—	20	—	—	20	—	10	—	—	—	10
468	95	20	—	—	—	20	20	—	—	—	—	20+
477	98	—	20	—	—	20	—	10	—	—	—	10
485	163	—	20	—	—	20	—	10	—	—	—	10
483	184	—	20	—	—	20	—	10	—	—	—	10
484	221	—	20	—	—	20	—	10	—	—	—	10
481	237	—	10	10	—	20	—	—	—	—	—	0
494	263	—	20	—	—	20	—	10	—	—	—	10
503	293	—	20	—	—	20	—	10	—	—	—	10
405	297	—	20	—	—	20	—	10	—	—	—	10
	323	—	10	10	—	20	—	10	10	—	—	20+
	332	10	10	—	—	20	10	—	—	—	—	10
	339	—	10	10	—	20	—	5	5	—	—	10
	343	—	10	10	—	20	—	5	5	—	—	10
	379	—	20	—	—	20	—	—	—	—	—	0
	399	10	10	—	—	20	5	5	—	—	—	10
	416	—	20	—	—	20	—	10	—	—	—	10
	195	10	—	—	—	10	—	—	—	—	—	0
	205	—	10	—	—	10	—	—	—	—	—	0
	238	—	10	—	—	10	—	—	—	—	—	0
	246	—	10	—	—	10	—	—	—	—	—	0
	276	—	10	—	—	10	—	—	—	—	—	0
	304	—	10	—	—	10	—	—	—	—	—	0
	364	—	10	—	—	10	—	10	—	—	—	10+
	376	—	10	—	—	10	—	10	—	—	—	10+
	386	—	10	—	—	10	—	—	—	—	—	0
	439	—	10	—	—	10	—	5	—	—	—	5
	441	—	10	—	—	10	—	—	—	—	—	0
	475	—	10	—	—	10	—	10	—	—	—	10+

+Indicates cases showing no improvement.

(2) Explanation of disability and reason for anxiety state. Attempts were made to get the patient to appreciate his disability and indicate how he might face up to it.

(3) Constant encouragement—realization of the difference between symptoms which are physiological and those which are pathological. By this is meant appreciation that excessive muscular action often produces stiffness and pain and that these can easily be corrected by graduated training at the same time as carrying out simple remedies such as contrast baths, massage and manipulation of affected parts by the patient himself.

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A Modified Smith-Petersen Nail for Fractures of the Neck of the Femur.—W. H. GERVIS, F.R.C.S.

The ordinary Watson-Jones type of nail has the disadvantage that it may slip out with consequent re-displacement of the fracture (fig. 1).

To prevent this the nail has been further modified by Pidcock by means of a cross pin at the base and Brittain and Corry by means of snagged edges at the base. In many cases the results with such nails are perfectly satisfactory.

Fixing the nail at the base has the disadvantage that it does not allow for impaction to occur. It has been stated that impaction only occurs as a result of avascular necrosis, but in cases observed there has been no evidence of this complication.

Should impaction occur the results may be serious for the point of the nail will be forced into the acetabulum (fig. 2).

Another possible complication is non-union (fig. 3).

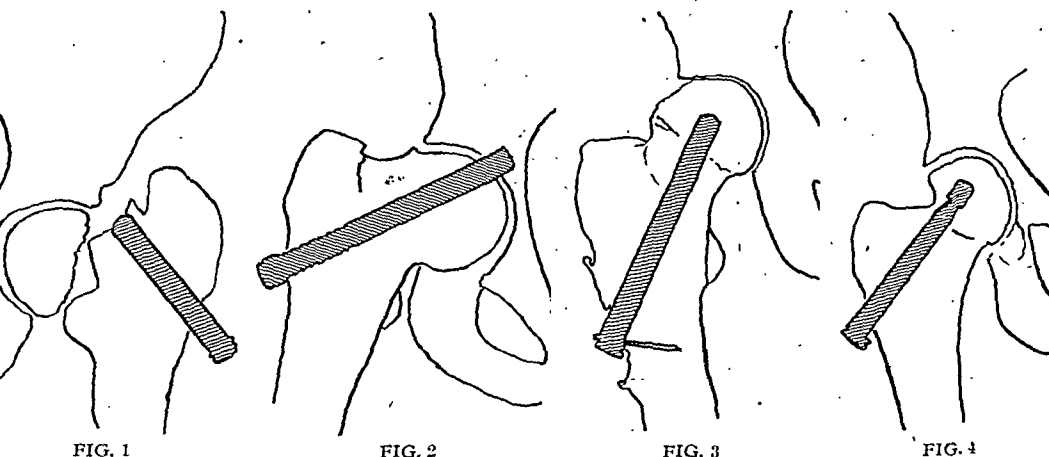


FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIG. 1.—A Watson-Jones type of nail that has slipped out.

FIG. 2.—To illustrate possible results of fixing the nail at the base. Impaction has occurred with penetration of nail into acetabulum.

FIG. 3.—Non-union. An uncommon result of fixing nail at base.

FIG. 4.—The nail described, with notches cut near point. These have fixed the nail in the head of the femur, impaction has occurred and the base of the nail has been extruded without harm.

This is not very clearly shown in the radiograph, though there is some periosteal reaction about the base of the nail. Clinically the non-union was quite definite, and when the patient walked her hip clanked (somewhat suggestive of the gait of a knight in armour).

To obviate these disadvantages a nail was tried with a notch cut in each flange a quarter of an inch from the point. It was hoped that these would fix the point of the nail in the head of the femur, and yet allow the base to extrude if impaction occurred (fig. 4).

This nail has been tried out in 25 cases and so far proved satisfactory in that respect. Removal of the nail after union has occurred has presented no difficulties.

A One Screw Technique in Oblique Fractures of Tibia.—W. H. GERVIS, F.R.C.S.

Fractures of the lower third of tibia are usually oblique, difficult to reduce and maintain in position, and as a result slow in uniting.

Internal fixation is therefore the ideal treatment and the use of one screw has long been practised and advocated.

Fixing a bone with a screw is merely a form of carpentry, and to do good carpentry the wood must be fixed in a vice or clamp.

This principle is carried out by reducing the overlap by means of a Steinman's pin in the os calcis and maintaining the traction with the leg hanging vertically over the end of the table during the operation. The fracture is then exposed, the fragments gripped by Lane's bone-holding forceps, and a perfect anatomical fit can be obtained and one screw inserted.

If the fracture is then stable, as it will be if the screw is correct, the skin is sutured, and a below-knee plaster cast, padded anteriorly, applied. When this has set the traction is released, and the cast continued above the knee.

By this technique the operation is simple and quick. Of more importance is the fact that there is the absolute minimum of manipulation and trauma to the tissues.

Intramuscular Vascular Patterns in Man

By L. B. BLONFIELD

Department of Anatomy, University of Oxford

RECENT experimental work on the vascularization of muscles in rabbits (Le Gros Clark and Blomfield, 1945) showed that, in spite of the presence of numerous arterial anastomoses, ligation of one of the main vessels at its site of entry, or interruption of a main intramuscular channel by an appropriate incision in the muscle or by a gunshot wound, may lead to sharply defined areas of ischaemia with ensuing necrosis. As the result of the evidence offered by these experiments, attention has now been turned to the intramuscular vascular pattern in human muscles and an attempt made to correlate the variations of pattern in different muscles with the liability to regional necrosis and anaerobic infections following injury. In spite of some early work by Wollenberg (1905) and some observations recorded in 1919 by Campbell and Pennefather, very little seems to be known of the course, distribution and anastomotic connexions in the different human muscles.

Radio-opaque media were injected into the main limb vessels of cadavers and the individual muscles dissected out, removed and X-rayed. In order to obtain a satisfactory injection it was found necessary to use a double injection technique, first ensuring the filling of the small vessels with a fluid barium suspension, and then filling the larger arteries with a mixture of barium sulphate paste and collodion. The main limb artery with the muscles supplied by it were then removed together in a single group, and the whole preparation X-rayed.

The vascular pattern in human muscles varies considerably from muscle to muscle, and these variations are clearly of importance in relation to their vulnerability. As an example, reference may be made to the muscles of the anterior tibial compartment. Both the tibialis anterior and the extensor longus digitorum contain a series of anastomotic loops formed by a succession of entering vessels, which extend through the whole length of the muscles. In each case there is a major anastomotic loop in the upper portion of the muscle and a succession of lesser arches below. Many subsidiary collateral anastomotic loops rise from the main loops, forming a complicated series of anastomosing arcades. But, while the tibialis anterior derives its blood supply entirely from the anterior tibial artery, the extensor longus digitorum also receives an abundant supply from perforating arteries which pass through the interosseous membrane from the posterior compartment of the leg. The extensor longus hallucis also derives its supply partly from perforating vessels as well as directly from the anterior tibial artery, but the former source is relatively meagre. Moreover, in this muscle the vessels form an open, quadrilateral type of pattern in which the anastomoses are much finer and evidently much less efficient than in the other muscles. In connexion with these differences it is interesting to note that some cases have been recently observed by Mr. Zachary (1945) from the Wingfield-Morris Orthopaedic Hospital, Oxford, in which, following oedema or haemorrhage into the closed anterior tibial compartment, the tibialis anterior and extensor longus hallucis both underwent necrosis, while the extensor longus digitorum was spared.

An interesting contrast is shown in the intramuscular vascular pattern of gastrocnemius and soleus. The pattern in both is formed mainly by longitudinally disposed vessels. But whereas in gastrocnemius the vessels are commonly derived from a single main artery which splits up into branches to enter the upper end of the muscle and descend throughout its entire length, in the soleus there are at least five separate vessels entering the muscle separately in succession from above downwards and contributing to the longitudinal anastomotic chain. This difference would account for the greater susceptibility of the gastrocnemius to anaerobic infections in wounds of the calf. For example, Trueta (1943) has informed me of a case with multiple wounds of the calf, involving both gastrocnemius and soleus, in which the whole of the former muscle had become converted into a necrotic mass while the underlying soleus retained its vitality. A similar case, in which the vessels entering the upper end of gastrocnemius were interrupted by a shell fragment leading to necrosis of the distal part of the muscle, has quite recently been recorded by Wood Power (1945).

From our studies it is possible to recognize five main types of intramuscular vascular pattern. These are as follows: (1) A longitudinal anastomotic chain formed by a succession of separate nutrient vessels entering the muscle throughout most of its length, e.g. soleus and peroneus longus. (2) Longitudinal pattern of vessels derived from a single group of arteries which rise from a common stem and enter one end of the muscle, e.g. gastrocnemius. (3) Radiating pattern of collaterals which rise from a single vessel entering the middle part of the muscle, e.g. biceps brachii. (4) A pattern

formed by a series of anastomotic loops ranging throughout the length of the muscle and derived from a succession of entering vessels, e.g. tibialis anterior, extensor longus hallucis and the long flexors of the leg. (5) An open quadrilateral pattern with sparse anastomotic connexions, e.g. extensor longus hallucis.

A preliminary survey of the relative vulnerability of muscles to necrosis and clostridial infections indicates that this may be related to the following vascular factors.

(1) The site of entry and source of the main nutrient vessels. Thus the gastrocnemius is particularly vulnerable since it is supplied by a single group of popliteal arteries which may all be involved in a local wound in the lower part of the popliteal fossa. The tibialis anterior is vulnerable to wounds involving the anterior tibial artery from which it derives its entire supply. The biceps brachii commonly has a single entering nutrient artery (see the case reported by Wood Power in which this vessel was interrupted by a shell wound).

(2) The number of nutrient vessels derived from independent sources.

(3) The intramuscular pattern of vessels. The longitudinal pattern characteristic of gastrocnemius and soleus renders these muscles more vulnerable to injury than the pattern of anastomotic loops in the long flexors and extensors of the leg.

(4) The efficiency of the intramuscular anastomoses. This is obviously less in the extensor longus hallucis than in the other long extensors of the leg, and there is clinical evidence that in progressive or mild degrees of ischaemia this muscle may undergo extensive fibrosis while the other muscles are relatively unaffected, as reported by Cohen (1945) at a recent meeting of the Vascular Injuries Committee of the Medical Research Council.

(5) The relation of the muscle volume to the size of the main nutrient vessels and the size of the anastomotic connexions. Both soleus and peroneus longus have a simple longitudinal anastomotic pattern formed in each case by about the same number of entering vessels. But the peroneus longus is much smaller in volume compared with the number and size of the vessels, and is almost never involved in anaerobic infections.

The investigations of which the results have been briefly outlined were carried out in the Department of Anatomy, University of Oxford, under the direction of Professor Le Gros Clark. The radiological records were made at the Radcliffe Infirmary with the kind assistance of Dr. Kemp, and the post-mortem material was made available by the help of Dr. Robb-Smith.

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A Case of Pathological Dislocation of the Hip—and What Happened to an Epiphyseal Transplant.—A. S. BLUNDELL BANKART, F.R.C.S.

Girl, aged 19. At the age of 3 months she had acute septic arthritis of the left hip. An abscess was opened and she recovered with the loss of the whole of the head and neck of the left femur. When first seen at the age of 2½ years, there was a pathological dislocation of the left hip, the greater trochanter was on a level with the anterior superior spine of the ilium, and the child walked with a pronounced limp.

On December 18, 1930, when she was 4 years 9 months old, a shelf operation was done and a large flap of bone was turned down from the ilium. At the same operation the upper 3 or 4 in. of the left fibula were excised and inserted as a graft into the trochanter at approximately the normal angle of a femoral neck. The proximal end of the graft carrying the fibular epiphysis was placed in the hip-joint, and the wound was closed. Skiagrams taken after this operation show that the fibular bone graft was absorbed and disappeared completely, but the epiphysis survived and has grown ever since.

During the next four years it was noticed that the upper end of the femur was tending to shift towards the outer side of the shelf, the epiphysis occupying most of the space between it and the acetabulum. On March 8, 1935, when the child was 9 years old, in order to improve the stability of the hip, a high subtrochanteric osteotomy was done and the shaft of the femur was placed directly under the fibular epiphysis. Since then the epiphysis has continued to grow and it has become more and more like the head of a femur. Skiagrams taken at the present day, fifteen years after the original transplantation, show that the epiphysis is completely ossified, that it is considerably larger than a normal fibular epiphysis of the same age, and that its upper border corresponds closely to the contour of the acetabulum above it.

The hip is now quite stable, there is 1½ in. of shortening which has not increased in ten years, and when this is compensated for, the patient walks with very little limp.

Section of Laryngology

President—C. GILL-CAREY, F.R.C.S.ED.

[May 4, 1945]

CLINICAL MEETING.

Eleven Cases Presented after Laryngectomy: Ability to Talk.—LIONEL COLLEDGE.

The President congratulated both Mr. Colledge and those who had taught the patients on the superb result. He could not think of any of his own patients who could compete with those of Mr. Colledge. He would like to ask Mr. Colledge how he set about teaching them, and whether they had lessons before the operation, as had been advised in certain quarters.

Norman Patterson had himself tried and failed to accomplish what Mr. Colledge had succeeded in doing, although he had carried out numbers of laryngectomies.

Musgrave Woodman said the mutilating effect of the operation had brought discredit on laryngectomy, but if patients could produce such a voice as did those of Mr. Colledge that feeling should disappear. Many cases of the kind in question went into the hands of radiologists and radium experts, but he thought that the operation should still have its place in surgery. He had treated a fairly large number in his time, and he could not remember any where the voice was so good as in Mr. Colledge's cases.

J. C. Hogg said he had learned a great deal from this excellent series of cases. On talking to them he had learned that apparently there was no need for any elaborate or specialized teaching afterwards; in fact, they very kindly told him that the secret of the whole thing was a bottle of soda water and a boiled sweet to suck.

E. Cowper Tamplin said that his experience had been that patients treated by radium or deep X-ray were usually fairly miserable. Mr. Colledge's, on the other hand, were a happy, laughing crowd, and that was one very striking difference, of great importance to the patient. Another point, to which Mr. Colledge himself had drawn attention, was that the hemi-laryngectomy case did not talk as well as the "total".

Lionel Colledge, in reply, said the President has asked how the patients were taught. Some taught themselves, some were taught by Mr. MacMahon, and some were taught by the ward sister who had been present that afternoon. The fact that they could talk was nothing new. He saw in 1914 in the clinic of Professor Gluck a man who talked very well, but he was looked on as a *lusus naturæ*. All efforts at that time to get patients to talk were devoted to producing an instrument by which they could talk; but gradually it had been found that nearly all the patients—not quite all—could be made to talk without any artificial aid, and gradually the artificial larynx had been dropped. They simply swallowed air and produced vibrations in the pharynx by belching.

The essential point was that they must produce vowel sounds if they were going to talk intelligibly. The vowel sounds were produced in the larynx and the consonants by the lips and tongue. If patients just whispered, the sounds which they produced were without vowels and were largely unintelligible.

He did not think that it was either feasible or necessary to train them before the operation. It had been recommended by an American writer recently, who suggested that three or four days should be taken up in training them beforehand. An effervescing drink helped beforehand, but when the cricoid was in position the pressure produced by the cricoid drawn back by the inferior constrictor made it very difficult, and the method of talking adopted was very much easier without a larynx. A patient who had been operated on three weeks ago went home a day ago and was beginning to talk already almost as well as any of the patients who had given the demonstration.

The President said the demonstration had been most stimulating. It had occurred to him that it might be tiring to the patients to produce their voice, but he had asked several of them and they assured him that they did not find it so.

Ligature of the Internal Maxillary Artery through the Antrum for Uncontrollable Epistaxis (Specimens and Instruments).—E. D. D. DAVIS.

E. D. D. Davis said that it was very rare to have to tie the internal maxillary artery. It was a good surgical maxim to attack the bleeding point and if ligature of a main artery was necessary it should be done as near the bleeding point as possible. He had ligatured this artery only once in a case of uncontrollable epistaxis. About six years ago a patient had nearly died of severe epistaxis and he thought the bleeding point was at the posterior end of the middle turbinal. The patient survived but after an interval of four years he had another severe epistaxis and the hæmoglobin was reduced to 38%. He tied the internal maxillary artery through the antrum then. The patient made an excellent recovery in spite of arteriosclerosis and had had no epistaxis for more than twelve months. The internal maxillary artery may have to be ligatured to arrest hæmorrhage after an injury or to control bleeding during nasal operations. It had been tied on many occasions to diminish hæmorrhage during nasal operations but he himself had never found it necessary for this reason. Some years ago it was the custom to ligature the external carotid before removing a growth of the maxilla but in his experience this procedure made no appreciable difference to the amount of hæmorrhage.

formed by a series of anastomotic loops ranging throughout the length of the muscle and derived from a succession of entering vessels, e.g. tibialis anterior, extensor longus hallucis and the long flexors of the leg. (5) An open quadrilateral pattern with sparse anastomotic connexions, e.g. extensor longus hallucis.

A preliminary survey of the relative vulnerability of muscles to necrosis and clostridial infections indicates that this may be related to the following vascular factors.

(1) The site of entry and source of the main nutrient vessels. Thus the gastrocnemius is particularly vulnerable since it is supplied by a single group of nutrient arteries which may all be involved in a local wound in the lower part of the popliteal fossa. The tibialis anterior is vulnerable to wounds involving the anterior tibial artery from which it derives its entire supply. The biceps brachii commonly has a single entering nutrient artery (see the case reported by Wood Power in which this vessel was interrupted by a shell wound).

(2) The number of nutrient vessels derived from independent sources.

(3) The intramuscular pattern of vessels. The longitudinal pattern characteristic of gastrocnemius and soleus renders these muscles more vulnerable to injury than the pattern of anastomotic loops in the long flexors and extensors of the leg.

(4) The efficiency of the intramuscular anastomoses. This is obviously less in the extensor longus hallucis than in the other long extensors of the leg, and there is clinical evidence that in progressive or mild degrees of ischaemia this muscle may undergo extensive fibrosis while the other muscles are relatively unaffected, as reported by Cohen (1945) at a recent meeting of the Vascular Injuries Committee of the Medical Research Council.

(5) The relation of the muscle volume to the size of the main nutrient vessels and the size of the anastomotic connexions. Both soleus and peroneus longus have a simple longitudinal anastomotic pattern formed in each case by about the same number of entering vessels. But the peroneus longus is much smaller in volume compared with the number and size of the vessels, and is almost never involved in anaerobic infections.

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Lionel Colledge thought it might be regarded as a basal-cell carcinoma.

Extensive Pharyngeal Ulceration.—IAN ROBIN.

W. G., male, aged 24. Extensive pharyngeal ulceration with necrosis of the soft palate and fauces was first noticed over three years ago. Very little change in the clinical condition in the past two years. Chest: X-ray normal. Blood W.R. negative. Three biopsies have all shown "simple granulation tissue only". Swabs have grown on culture *Staph. aureus* (penicillin-sensitive), and non-haemolytic streps. Blood vitamin C content normal. Blood-count shows simple "secondary anaemia" with Hb% varying between 50 and 85. For many years the patient has suffered from severe ulcerative colitis. This has been treated medically, and also by appendicostomy. X-rays of the colon show marked "pipe-stemming". The small firm gland in the right side of the neck has been present for at least seven years. The patient suffers also from infantilism, for which he has received various hormones.

Treatment of the pharyngeal condition has included local and parenteral arsenic; local and parenteral penicillin; large doses of vitamin C; iron; frequent blood transfusions; nearly all of the sulphonamides both locally and by mouth.

The patient is now awaiting admission to hospital for an ileostomy, and subsequent colectomy.

V. E. Negus said he had at the present time a case of a similar type under his care; and he had seen one or two in the past. Some had been spoken of as malignant granulomata and others had been given various names. The man he had in mind came from the Army in North Africa, but there had never been an accurate diagnosis. The condition was not syphilitic nor tuberculous nor was it reticulosis. It improved a little with penicillin, which was given both by injection and in pastilles, but it improved only because that got rid of the secondary penicillin-sensitive organisms. It extended over much the same area as Mr. Robin's case. The patient was now having intrabuccal irradiation; the ulceration appeared to be healing rapidly. Although it might theoretically be the wrong treatment for an inflammatory process there did seem to be a good result. Diathermy was not a good form of treatment in this case, though it had been tried.

G. Ewart Martin said he had seen three almost identical cases. So far they must admit failure in diagnosis of these cases. A tentative diagnosis of reticulosis was made in two cases but he was certain this was incorrect. The third case, a woman of 28, developed a small ulcer on the side of the tongue making swallowing painful. The ulceration continued and eventually the tongue split in two. Serial sections apparently showed simple granulation tissue and every possible blood test had been negative. There was no definite agranulocytosis. The patient became pregnant, the baby was born without any difficulty and was perfectly healthy. The ulceration continued slowly causing a great deal of pain on swallowing. The patient lost and gained weight alternately. Deep X-ray therapy was tried and the upper part of the ulcer healed but it appeared on the posterior pharyngeal wall, passing down as far as the epiglottis. A superficial ulcer appeared on the skin over the thyroid cartilage. Pus from this ulcer showed no definite infection and it eventually healed with deep X-ray therapy. The blood-count has varied. For some time there was a general anaemia and this responded to blood transfusions. Since five blood transfusions were given the ulcer has been partly controlled. The patient was very bright and had put on weight but talking and swallowing were difficult. The diagnosis had failed.

Carotid Body Tumour.—IAN ROBIN.

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Diagnosis of carotid body tumour made. In September 1944 Mr. Hamilton Bailey excised the tumour, after preliminary ligature of the carotid artery. The tumour was well encapsulated, but extended up to the base of the skull, and actually had to be "chipped off" the bone.

Microscopy confirmed the nature of the tumour.

Bilateral Abductor Palsy Following Thyroid Operation Two Years Ago.—N. A. JORY.

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V. E. Negus said that Sir StClair Thomson, who had strong views on the subject, advocated permanent tracheostomy. If the patient had a properly constructed tube, of the right shape, and if that tube were properly shaped at the outer end, it was possible to have it made with a valve which gave a wide aperture. The valve did not then project; such tubes were now made and were very convenient because they were out of sight. There was also very little trouble in inserting one into the trachea.

Caesar Hirsch had ligatured the internal maxillary artery through the antrum on three occasions for uncontrollable epistaxis.

The specimens and instruments shown illustrated the technique clearly. The small aneurysm needle was recommended and ligation through the antrum was not difficult.

Surgeon Commander Passe had ligatured the internal maxillary artery six times. He tied the artery at the posterior border of the ascending ramus of the mandible as it emerges from the parotid gland five times. On the last occasion he made an incision in the mucosa of the mouth close to the tuberosity of the maxilla. The artery was found lying on the pterygoid plate and was pulled forward into the wound by a hook.

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Norman Patterson asked what the advantage was in tying the internal maxillary as compared with the external carotid. In a case of very severe hæmorrhage after operation on the antrum, he said, the external carotid was ligatured and the bleeding stopped at once. It was comparatively easy to tie. It did, however, leave a scar on the neck. He could not see the advantage of the complicated procedure described when it was possible to tie the external carotid. Some years ago he found out that it was easier to ligature this vessel by making an incision in the posterior part of the sheath, drawing the internal jugular forwards and inwards, and getting access to the artery from behind rather than from in front. It was not necessary to sever any veins at all.

R. G. Macbeth said that there had recently been a number of cases of the type mentioned by Mr. Davis at the hospital for head injuries, St. Hugh's College, Oxford, and there they had found it easy to control the situation by tying the anterior ethmoidal artery in the orbit.

E. D. D. Davis (in reply to Mr. Patterson): Whenever I have ligatured or seen the external carotid ligatured for growths of the maxilla it has had no appreciable effect on the bleeding. The result of this ligature on the hæmorrhage can be tested by applying and releasing a clip placed on the artery. The last time I ligatured the external carotid it took three-quarters of an hour. It was difficult because the common carotid bifurcated high up in the neck and it was surrounded by a plexus of veins.

Ligature of the internal maxillary artery through the antrum is easier. It can be done in twenty minutes and it has the advantage of being nearer the bleeding point. For example it is better to ligature the anterior and posterior ethmoidal arteries for epistaxis than the internal carotid.

Tumour of the Left Ethmoid.—MYLES L. FORMBY.

Signalman A. P., aged 18. October 1943 complained of watering from the left eye. Lacrimal duct probed and dilated. April 1944 he is reported to have had a small cystic swelling in the region of the inner canthus of the left eye and a smaller and harder swelling on the infra-orbital margin at its inner extremity. In December 1944 the swelling had increased slightly but the lacrimal duct was said to be patent. There was a fluctuant swelling near the inner angle of the left orbit from which a few drops of watery mucus were aspirated. Culture yielded pneumococci and Koch-Weeks bacilli. This swelling did not appear to communicate with the lacrimal sac. Anterior rhinoscopy revealed a vascular mulberry-like tumour in the anterior part of the left middle meatus. Histological examination of a portion removed at biopsy was reported as showing "widespread and generalized invasion with well-defined columns of cells some spindle-shaped, with little cytoplasm and hyperchromatic nuclei, with few mitotic figures which are malignant and a few lymphocytes surrounding but not infiltrating the malignant cells".

An external ethmoidectomy was performed on February 12, 1945. The swelling was found to be firm, projecting through the lamina papyracea and everting the nasal process of the maxilla. It separated readily from adjacent structures but no trace of the lacrimal sac could be identified. The opening into the nasal cavity was enlarged, and a mass of firm but soft polypoid tissue was removed from the ethmoid region. The left middle turbinal was found flattened against the nasal septum. The tumour appeared to originate in the lateral mass of the ethmoid and to displace, without infiltrating, adjacent structures.

Microscopically the growth consisted of groups of closely packed cells with small spherical nuclei and little cytoplasm. The groups are separated by a fibrous stroma. Mitoses are few. In some parts of the section there was definite evidence of infiltration and the growth is histologically malignant.

It was quite definite from the section that the tumour was malignant. It was growing in a manner which suggested that it was rather pushing structures out of the way, and if it was malignant it was only locally malignant. If it was a carcinoma it was surprising, because the patient was only 18½ years of age. It was just three months since the patient was operated on, and they proposed to let him go another three months unless any member had an alternative suggestion to make and a convincing reason for doing otherwise.

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H. V. Forster said that he had had referred to him a case like the one under discussion. The bilateral abductor palsy had followed an operation on the thyroid gland. He saw the patient from time to time, but remembering the teaching of the late Sir StClair Thomson, would continue to encourage her to wear her tracheotomy tube and not to submit to any kind of intralaryngeal operation.

J. C. Hogg said that he agreed with what speakers had said with regard to permanent tracheotomy tubes. He had a patient who had this disability after a thyroid operation and in due course he had fitted her up with a flap valve which had enabled her to speak but she had refused to go on with it because she could breathe in through it but owing to paralysis of the cords she could not breathe out properly. She decided that it was not good enough and she put a finger on her tracheotomy tube and one would not have known that she had a disability at all.

Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN LONDON

[June 1, 1945]

LARYNGOLOGICAL SESSION

Chairman—C. GILL-CAREY, F.R.C.S.Ed.

(President of the Section of Laryngology)

External Operation on the Nasal Sinuses

By NORMAN PATTERSON

THE operation is designed to give an adequate exposure of the ethmoidal cells, sphenoidal sinus, and maxillary antrum by means of an external route of approach. The skin incision is made in the line of the naso-jugal fold and the resulting scar is practically invisible. The method of approach possesses the advantage, so far as the maxillary antrum is concerned, of avoiding a route, as in the Caldwell-Luc operation, through the cavity of the mouth which is always more or less septic.

Since bringing the maxillary antrum into the compass of the operation I have found that not only exposure of the lacrimal duct, but free mobilization of this structure by removing the bone which surrounds it is necessary if the operation is to be thoroughly and successfully carried out.

Nearly all the patients subjected to operation have suffered from extensive polypi; frequently the antrum has also been involved, often being filled with polypi. Most of the patients had already undergone several unsuccessful operations.

The skin incision begins immediately below and external to the internal canthus and follows the naso-jugal fold in an outward and slightly downward direction for about an inch. The skin should be sliced rather than cut vertically to its surface and if the incision is made slightly wavy the best cosmetic result is obtained. After making the incision the eyelids are brought together by two or three stitches to avoid injury to the conjunctiva.

The fibres of the orbicularis oculi are separated with a blunt dissector till the infra-orbital margin is exposed. At this stage it is advisable to insert a stitch of strong material through the skin and soft tissues just internal to the inner end of the skin incision; this prevents tearing when the sides of the wound are retracted.

The periosteum is now incised immediately below the infra-orbital margin making sure that this membrane is divided right down to the bone; it can now be elevated from the upper part of the anterior surface of the maxilla bearing in mind the position of the infra-orbital foramen. The upper part of the ascending process of the maxilla is denuded of periosteum, care being taken not to interfere with the attachment of the internal tarsal ligament. The periosteum is elevated from the anterior and inner part of the floor of the orbit. It is now possible using a sharp gouge to remove a small portion of the lower orbital margin and so bring into view the muco-periosteum in the region of the anterior superior angle of the maxillary antrum. The antrum can now be opened. At this stage a swab should be taken for subsequent bacteriological examination.

The next step is to expose the outer surface of the lacrimal duct by removing bone from the neighbourhood of the lower part of the lacrimal groove. A piece of bone often comes away bearing the impress of the lacrimal duct. The antrum may now be

exposed freely by removing more bone. It is well to postpone any surgical treatment of the antrum till a later stage in the operation. The next step is to remove all bone and cells lying in proximity to the anterior internal and posterior aspects of the upper part of the lacrimal duct; it is important not to proceed too far in the direction of its nasal orifice as there is a danger of detaching the duct from its lower attachment. The upper portion of the duct is now mobilized and it is possible so to displace it as to facilitate carrying out the further stages of the operation. Diseased ethmoidal cells and polypi are frequently found in front of the duct extending nearly up to the anterior nasal angle.

The next stage in the operation is to elevate the periosteum covering the inner wall of the orbit, upwards towards the base of the skull and backwards nearly as far as the posterior limit of the orbital cavity; the proximity of the optic nerve must be kept in mind. By employing a suitable retractor the orbital periosteum together with the contents of the orbit can be displaced outwards and slightly upwards. Removal of the lower portions of the ethmoid, including cells and orbital plate, can be accomplished without danger, great care, however, must be taken when the region of the sphenoidal sinus is approached and special caution is necessary in dealing with the upper part of the ethmoid which lies in close proximity to the anterior fossa. The upper cells are roofed in by a very thin plate of bone and in opening these cells the forceps should be gently placed in position; no force is permissible. The forceps are closed and by gentle traction downwards and forwards the bony fragments are removed bit by bit until all the upper cells have been opened. The remaining depressions representing the roofs of the cells can best be cleared of mucous membrane or polypi by the use of pledgets of gauze held at the end of a pair of nasal dressing forceps. The sphenoidal sinus should be investigated and if the cavity is found to be diseased the natural ostium should be enlarged sufficiently to allow of free drainage.

The next procedure is to examine thoroughly the maxillary antrum and if sufficient bone has not been removed for this purpose more may be taken away. To illuminate the antral cavity the surgeon should change his position and stand at the head of the table directing the beam of light downwards and backwards. When the lining membrane is unhealthy it can be eliminated as thoroughly as when carrying out a Caldwell-Luc operation. In cases where the antrum is diseased the whole of its nasal wall above the inferior turbinate should be taken away so as to establish a large permanent opening. An opening in this situation is to my mind more effective than one situated in the wall of the inferior meatus.

This operation is not designed to deal with the frontal sinus but it is often possible to pass a probe into the sinus and not infrequently pus is seen to ooze from the neighbourhood of the fronto-nasal opening. Even in cases where there is chronic suppuration in the frontal sinus clearance of the ethmoidal region carried out sufficiently far forward and high up will sometimes result in so much improvement in drainage that there is a cessation of all frontal sinus symptoms. If, however, the disease in the frontal sinus persists that cavity should be opened through an incision which corresponds to the lower margin of the eyebrow. A final inspection, under magnification if possible, is carried out. I find that polypi may spring from the upper or ethmoidal portion of the nasal septum a point which has received little notice. In one case in order to effect a cure I had to take away the whole of the upper part of the septum.

It is necessary during the course of the operation to keep the cavity as free as possible from blood. A suction apparatus is essential aided by gentle swabbing. The head should be kept in a slightly elevated position. Hydrogen peroxide and weak adrenalin solution are useful hæmostatics. The cavity is finally dusted with sterilized sulphanilamide compound.

In closing the wound the orbicularis oculi is brought together with a few stitches of fine catgut. Ophthalmic thread is employed on a small curved needle to bring the edges of the skin together. The stitches are removed in from three to five days.

Recently I have on two occasions tried another incision which may prove useful to those who are nervous about any incision on the face. The incision corresponds to the margin of the lower eyelid and at the outer canthus it is carried outwards a little further in one of the creases nearly always present in this neighbourhood. A flap of skin is turned down so as to expose the orbicularis oculi and subsequently the operation proceeds as described.

This operation has led to much better results than I have obtained by other methods. Generally speaking instead of a large percentage of failures in cases of chronic nasal sinus disease associated with polypi I can now claim a very large percentage of successes. Complications have been few and generally insignificant. It is gratifying to see how many patients recover often after the loss for many years of their sense of smell and frequently of taste.

- (1) Total number of external sinus operations performed at the Royal Bucks. Hospital between December 1939 and March 1945.

	Total	73
Norman Patterson		44
S. W. Hargrove assisted by Norman Patterson		14
E. O. Harris assisted by Norman Patterson		15

73

- (2) Post-operative complications.

(a) Three cases of diplopia (in two of these cases a radical frontal operation was also performed).

(b) Epiphora—in the early series where the naso-lacrimal duct was not preserved, epiphora was permanent, varying in severity from case to case. In the cases where the naso-lacrimal duct was preserved there was transient epiphora which always cleared up.

(c) There were no other complications; the average stay in hospital for cases operated on under regional anaesthesia was seven days; under general anaesthesia eleven days.

(d) Three cases—polypi recurred and further operative treatment was performed, and it was found that the polypi were growing in two cases from the cells lying anterior to the naso-lacrimal duct.

- (3) In those cases in which smell was absent it returned in all but one.

- (4) Anaesthesia:

(a) General	19
(b) Regional	54

1 Statistics compiled by my Assistant Mr. S. W. Hargrove.

Anæsthesia for Surgery of Nasal Sinuses

By H. W. LOFTUS DALE

WE now only employ general anaesthesia in those cases which are temperamentally unsuited for regional methods such as children, adolescents and those with an unstable nervous system. The patients who require this operation are usually those most suitable for regional anaesthetics, the majority of them being between the third and sixth decade, many of whom have already undergone several intra-nasal operations under surface anaesthesia with cocaine, and have been agreeably surprised.

Since the discomforts incidental to the operation are not negligible, the length of time on the table, the face being covered with towels, the use of the hammer and chisel, nibbling forceps, &c., something more than complete abolition of pain sense is required, hence the important part played by premedication to which regional anaesthesia owes its increasing popularity.

Scopolamine in full doses tends to produce mental disorientation, particularly in older patients, and intense discomfort due to the drying up of secretions. The opiates produce a pleasant lethargy, a reasonable degree of general analgesia and amnesia giving a drowsy but co-operative patient, with sufficiently active reflexes to protect himself against the aspiration of foreign matter.

This state is best attained by the intravenous route, the action is rapid in onset, more intense, and of shorter duration, the maximum depressant effect on respiration and metabolism being reached in fifteen minutes, and analgesia in a matter of seconds, side-effects, such as vomiting, are much less frequent. This method is perfectly safe providing a few simple rules are observed.

Intravenous omnopon technique.—(1) If morphia or omnopon is given by the hypodermic route in the ward, at least one hour must have elapsed before giving an intravenous dose in order that the maximum depressant effect on respiration will have been reached. (2) The injection must be slow in order to see if any idiosyncrasy exists, and to avoid unpleasant subjective sensations, viz. feeling queer or dizzy, tinnitus, palpitation or dyspnoea. (3) Pauses should be made in order that the effect of the previous instalment is apparent before giving the next, in other words to give the signs time to develop. (4) The patient's respiration, colour and pupil should be watched; the minimum analgesic dose produces contraction. Speak to him and when his responses become slow and he shows signs of drowsiness, stop. It is better to give some more later if he becomes too alert than to produce undue depression with the initial dose.

Nembutal $1\frac{1}{2}$ grains three hours and $\frac{1}{3}$ grain of omnopon with $\frac{1}{150}$ grain of scopolamine one and a half hours before operation is given to the average patient; scopolamine is not given to those over 60.

The patient's response gives a fair idea of the intravenous dose likely to be required, which varies from 0 to 1 grain.

I use omnopon in 1 c.c. ampoules containing $\frac{1}{3}$ grain adding 2 c.c. of sterile distilled water for each ampoule used so that each 3 c.c. = $\frac{1}{3}$ of a grain, this dilution facilitates

slow injection, and shows at a glance how much has been given; constantly using the same dilution assists in correlating the dose and the time factor.

Nerve block.—The sensory innervation of the nose and sinuses is derived from the first and second divisions of the 5th cranial nerve. The ophthalmic nerve is not accessible at the base of the skull, but branches within the orbit are easily reached. The nasociliary nerve enters the orbit through the sphenoidal fissure, crosses the optic nerve obliquely between the superior and internal recti reaching the anterior ethmoidal foramen where it becomes the anterior ethmoidal nerve and can easily be reached at this site by the medial orbital route.

The maxillary nerve is accessible in the pterygo-palatine fossa; injections at this site are bound to include the spheno-palatine ganglion and efferent branches in the resulting zone of analgesia.

Five approaches have been described, three extra- and two intra-oral. (1). Through the incisura of the mandible just below the mid-point of the zygoma. (2) Through the angle formed by the anterior border of the coronoid process with the inferior margin of the zygoma. Both routes have been termed zygomatic. (3) Orbital route: Through the infero-lateral margin of the orbit following the floor and passing through the inferior orbital fissure. (4) Oral: (i) Through the mucous reflection above the first upper molar. (ii) With a needle or mount angled to 145 degrees introduced behind the last upper molar in a vertical direction at right angles to the upper occlusal plane.

I chose the first route for several reasons. Approach through the skin seemed to hold less risk of carrying infection to an area containing structures such as the pterygoid plexus of veins. The deep and superficial landmarks are easily identified and the angles of approach easier to estimate. Hematoma of the cheek is said to be a common complication of the second route. Deep orbital injections involve the risk of injuring or anesthetizing the optic nerve. The term mandibular is preferable to zygomatic for the route chosen, since confusion with the second route is avoided and the mandibular nerve can be blocked from the same point of entry.

Technique Block I.—With the patient supine, head sideways, affected side up, the depression, bounded by the inferior border of the zygoma and the incisura of the mandible, is palpated; identification is assisted by the patient opening and closing his mouth. Using a fine needle, a wheal is raised inferior to the mid-point of the zygoma, which corresponds with the centre of the depression. Through the centre of this wheal a 10 cm. needle, fitted with a rubber marker, is introduced transversely at right angles to the sagittal plane of the skull.

Bony contact at a depth of 4 to 5 cm. which should not be exceeded, indicates that the point is in contact with the lateral pterygoid plate. The marker is now set at a distance of $\frac{1}{2}$ to 1 cm. from the skin surface.

In order to change direction the needle is withdrawn until the point is free in the subcutaneous tissues, and is then reinserted at the angle of 20 degrees forwards and slightly upwards, so that the point is directed towards the pterygo-palatine fossa.

If no contact with bone is made when the marker again reaches the skin surface, connect the syringe to the needle and inject a few drops of the solution in order to see that the needle has not become blocked; aspirate to ensure that the point is not in a blood-vessel. If the aspiration test is negative 2 c.c. of the solution is slowly injected. If on reinsertion bony contact is made before the marker reaches the skin surface it means that the angle was too small to enable the needle to clear the pterygoid plate, withdraw and reinsert at a greater forward angle. Paræsthesias referred to the palate or upper molar region are common.

The absence of paræsthesias is not necessarily an indication of failure. The head is now straightened for the performance of **Block II Medial Orbital**: A 5 cm. needle is introduced below the eyebrow 1 cm. vertically above the inner canthus, keeping the bevel in close contact with the wall of the orbit at its superior and medial angle until a depth of 2.5 to 3 cm. is reached. The point should now be in the region of the anterior ethmoid foramen. The syringe is connected and if the aspiration test is negative 1 to 1.5 c.c. of the solution is slowly injected. The loose areolar tissue permits of rapid diffusion. If this technique is carefully carried out there is no danger to the contents of the orbit.

Analgesia appears in from three to fifteen minutes; testing by pin-pricks is unreliable in the pre-medicated patient. If the preliminary suture of the eyelids can be performed painlessly it may be assumed that both blocks have succeeded.

DRUGS AND TECHNIQUE

Drugs.—The action of procaine, also known as novocain, neocaine, ethocaine, may not be sufficiently sustained for the duration of this operation.

Anethaine, known variously as decicain, pontocaine, pantocaine, butethanol, amethocain, acts for much longer. It can be used alone or combined with procaine, which is said to enhance the advantages of both drugs. It is supplied in this country by Glaxo Ltd. under the name "anethaine".

Distrusting the traditional rubber-capped bottle of uncertain sterility, potency or pH, I prefer to make up my own solutions freshly as required. Recently, however, Messrs. Glaxo make for me 2 c.c. ampoules each containing: Procaine 40 mg., anethaine 2 mg. with adrenaline 1 in 400,000. These are etched to avoid infection arising from glue used for labels. This solution gives analgesia of rapid onset and sustained effect.

Pressure should always be exerted in the long axis of the needle to avoid bending or breaking. Marked paræsthesias before the injection is made suggest penetration of the nerve, intraneural injections may be followed by severe and persistent neuralgic pain. Paræsthesias coming on whilst the injection is being made indicate an accurate paraneural injection and the early onset of complete analgesia.

Repeated attempts are not justified since the injection of large amounts of fluids will, in either block, produce exophthalmos and anaesthesia of the entire contents of the orbit. For this reason I prefer to rely on the accurate placing of a small quantity of a strong solution rather than on the diffusion of a larger amount of a weak solution forced into the surrounding area.

There never has been complete failure to obtain analgesia, a very small number of patients have complained of pain during the operation and in these cases it was only for a short while, and limited to manipulations in a small area, and possibly due to traction on structures outside the zone of analgesia or an overlap of nerve supply from the opposite side.

Nearly all our patients have had bilateral operations and did not in the least mind facing the second one; one only, a highly-strung girl of 16, asked for a general anaesthetic for the second operation.

Complications have been few and minor, two patients complained of neuralgic pain lasting three to four days, and a few of paræsthesias and numbness.

Surgeon Commander E. R. G. Passe said that Mr. Norman Patterson had evolved a transorbital approach to the ethmoid labyrinth and the sphenoidal and maxillary sinuses. Since 1939 he, Surg. Cdr. Passe, had made use of this approach in this country and abroad, on 145 occasions, for the following conditions: chronic non-specific infections of the ethmoidal, sphenoidal, and maxillary sinuses; in conjunction with operations on the frontal sinus, for chronic infections of that sinus; drainage of an extradural abscess; drainage of an orbital abscess; in a case of retrobulbar sinusitis due to a large infected posterior ethmoidal cell; in malignant disease of the ethmoidal mass, and as one of the steps in excision of the upper jaw.

In order to obtain a less superimposed radiograph of the ethmoidal labyrinth, he had constructed from dental X-ray films, a film the shape of the old-fashioned septal splint, which under light cocaine anaesthesia could be inserted alongside the septum as high as the roof of the nasal cavity. Lateral pictures of each ethmoidal labyrinth were then obtained separately by directing the rays through the maxillary sinus.

For anaesthesia he preferred heavy premedication with nembutal and morphia, followed by simple packing of the nasal cavity with 5% cocaine and 1/1000 adrenaline. For the skin incision he infiltrated with novocain. This appeared also to give as dry a field as it was possible to obtain, and though in several cases a preliminary ligature of the internal maxillary artery as it left the parotid gland was performed, he had now abandoned this method as it had no very appreciable effect on the bleeding. Illumination in the depth of the field was sometimes a difficulty, and he had found that a small light on a malleable flex was of considerable help. Both sides of the nose could be operated on at the one operation.

Although it was known that many cases of intractable neuralgias of the first and second divisions of the 5th cranial nerve were due to infections of one or more groups of ethmoidal cells, rhinoscopy did not always reveal the disease. In these cases, it seemed to him, ethmoidotomy was as justifiable a procedure as any other exploratory operation.

The theory of Mr. Norman Patterson's operation in cases of chronic infection and polypoid degeneration was sound in that the infected and polyp-bearing area was removed so far as the ethmoid was concerned. The results which were uniformly good bore this out. Mr. Norman Patterson had given a great stimulus to nasal and accessory nasal sinus surgery with his new, safe, and direct approach to this area.

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The incision used fulfilled three desiderata: First, the lacrimal duct, literally surrounded by polypi, was in the middle of the incision. Secondly, as that anchor of the eye, the medial palpebral ligament, was left intact, no diplopia had ever resulted even temporarily. Thirdly, it gave an excellent entry to the maxillary antrum, which, in all 25 cases, was abounding in polypi, so that any radical operation must include the removal of the antral contents.

To avoid danger to the optic nerve, the level of the front wall of the sphenoidal sinus was the limit of the removal of the lamina papyracea.

The results of this operation were excellent: in these 25 cases no deaths resulted, nor were there any complications, which might be surprising in view of the enormous amount of bone removed.

V. E. Negus said that it would be a pity if this operation were accepted—as it probably would be on Mr. Patterson's recommendation—and were used broadcast. In Mr. Patterson's hands it might be very successful, but it was not an operation for all. He, Mr. Negus, had spent a lot of his time during the last few years in undoing some of the damage done to sinuses, and particularly the frontal sinus, and he thought there had been in the present discussion a tendency to ignore and forget the frontal sinus. It came back on one later.

In cases of polyposis with no infection this operation might give good results, but it seemed a very inconvenient route of approach. Most of them thought that they could eventually by an extended intranasal operation clear the patient's nose satisfactorily, and that the necessity for external operations for simple polyposis rarely arose.

This operation was going to be used for infection. If one operated on the ethmoidal cells where there was a sinusitis of long-standing and forgot the frontal sinus the patient was in for trouble. He thought it was fatal to clear the ethmoidal cells without making certain as to the provision of free drainage through a new fronto-nasal duct, which was probably either blocked at the time or would shortly become blocked.

What was the reason for this approach? It seemed to centre very much on facial disfigurement. If one made a correct scar in the more usual type of frontal sinus operation, starting just below the inner margin of the eyebrow, and curving round the inner margin of the orbit as far as possible from the canthus, no disfigurement followed. If there were disfigurement something had been done wrongly, either the incision had been made through the eyebrow or too close to the canthus.

They had heard just now that the naso-lacrimal duct was surrounded by polypi. He thought that was incorrect. The ethmoidal polypi were inside the orbital plate of the ethmoid. If one lifted up the orbital periosteum cleanly, the polypi would all be on the inner side. If the orbital plate of the ethmoid were removed it was possible to remove the cells much more cleanly than by the lower approach, and open the sphenoidal sinus and drain it with safety.

He hoped that if this operation was going to be used it would be in an extremely limited number of cases of polyposis without infection.

Mr. Walter Howarth: I went to see Mr. Patterson perform this operation at Aylesbury and watched it with great interest. I have tried it myself several times and I have come to the conclusion that it is a highly dangerous operation except in hands as skilled as those of Mr. Patterson. The operation seemed to me to be directed towards the cribriform plate which is the danger area of the nose, instead of towards the fronto-nasal duct. Moreover it entirely failed to expose the fronto-ethmoidal cells and so drain the frontal sinus. I regard this as a very great defect of the operation, as even if the ethmoid is thoroughly cleared out it is essential to deal with the fronto-nasal duct and so drain a possible frontal sinusitis.

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Norman Patterson said that his feeling was that if one looked after the ethmoid, the frontal sinus in a large majority of cases would take care of itself. The reason for persisting suppuration in a frontal sinus was very often due to the fact that drainage was interfered with on account of the presence of ethmoiditis, generally of the polypoid variety.

He agreed that it was a difficult operation to perform; it required a good deal of dexterity, and an intimate knowledge of the anatomy of the region.

It is the lacrimal sac which lies in the orbit, not the duct. He thought the duct was the key to the situation. In a good many of his cases chronic infection was present and practically all were associated with extensive polypi. There had been no evidence of blockage of the fronto-nasal duct as suggested by Mr. Ewart Martin. Results proved the operation to be practically free from danger. Free access to the antrum as well as the ethmoid and sphenoid was one of the great advantages of the operation.

[June 2, 1945]

Primary War Injuries Involving the Nose and Sinuses

By Colonel NORTON CANFIELD, M.C., A.U.S.

DURING the feverish activity of the past two years, the members of our specialty have been occupied chiefly with the application of well-known and recognized principles of therapy. A few have had the opportunity for investigation of new ideas and advancing lines of thought. Some of this work has been reported but much of it is still to be presented. Masses of statistical data are available on the usual conditions of otitis media, sinusitis, pharyngitis. Final reports on blast ears and the resulting damage to hearing are in the process of being assembled.

In addition to these there is a significant group of cases which will continue to come under the observation of the otolaryngologists as time passes. The acute injury presents a picture to the forward surgeon which from now on we will see but rarely in this theatre of war. Fortunately the repair processes start at once and when the danger of infection has passed, healing around the head is rapid and progresses in an excellent manner.

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He agreed that it was a difficult operation to perform; it required a good deal of dexterity, and an intimate knowledge of the anatomy of the region.

It is the lacrimal sac which lies in the orbit, not the duct. He thought the duct was the key to the situation. In a good many of his cases chronic infection was present and practically all were associated with extensive polypi. There had been no evidence of blockage of the frontal-nasal duct as suggested by Mr. Ewart Martin. Results proved the operation to be practically free from danger. Free access to the antrum as well as the ethmoid and sphenoid was one of the great advantages of the operation.

[June 2, 1945]

Primary War Injuries Involving the Nose and Sinuses

By Colonel NORTON CANFIELD, M.C., A.U.S.

DURING the feverish activity of the past two years, the members of our specialty have been occupied chiefly with the application of well-known and recognized principles of therapy. A few have had the opportunity for investigation of new ideas and advancing lines of thought. Some of this work has been reported but much of it is still to be presented. Masses of statistical data are available on the usual conditions of otitis media, sinusitis, pharyngitis. Final reports on blast ears and the resulting damage to hearing are in the process of being assembled.

In addition to these there is a significant group of cases which will continue to come under the observation of the otolaryngologists as time passes. The acute injury presents a picture to the forward surgeon which from now on we will see but rarely in this theatre of war. Fortunately the repair processes start at once and when the danger of infection has passed, healing around the head is rapid and progresses in an excellent manner.

The advent of effective chemotherapy has probably been our greatest aid in war wounds and gradually as we discover its limitations we shall see it in proper perspective. It is now firmly established that a proper blood concentration of sulphadiazine and penicillin does prevent the spread of infection into healthy tissues if the patient's general condition is good. These agents do not completely prevent infection from developing in the wound and are not a substitute for surgical attention to the traumatized region.

The drama associated with facial wounds tends to put the emphasis upon appearance of the patient and the considerations of internal anatomy and physiology of the nose, sinuses and pharynx are too often disregarded in spite of the warnings of the otolaryngologists. The exigencies of war can never be adequate reason for failure to pay the strictest attention to the field of the rhinologist. To be sure, many cases will require plastic repair, but the upper-respiratory comfort of the patient will be a lifelong consideration, long after the plastic surgeon has completed his final repair.

Photographic methods have so improved that we can now present these cases as they originally were seen in the Army hospitals. All these which are shown at this meeting were taken within approximately ten days of injury and are typical of thousands which occur in modern warfare. One wonders why the face is not better protected when the known danger produces such specimens.

In the handling of these cases certain principles emerge and should be observed: (1) Anti-bacterial chemotherapy is of definite benefit in keeping undamaged tissue healthy. (2) Wounds of the face heal extremely well. (3) Foreign bodies which interfere with healing and function should be removed. (4) Thorough débridement of the wound is essential. This demands that the para-nasal sinuses be completely cleaned and drainage provided for later irrigation. If débridement is not done primarily it must be done before the final plastic repair. (5) Primary suture of the tissues produces excellent results, *providing* the débridement has been adequate. (6) If the loss of tissue is excessive primary treatment should consist of débridement and skin traction to prevent further gaping of the wound, leaving any definitive treatment till the inflammatory phase and local infection have subsided.

Col. Canfield showed 21 coloured lantern slides and commented on various features of the individual cases: (1) The use of tracheotomy in war wounds of the face and neck. (2) Different types of wounds from various types of missiles. (3) Foreign bodies in the sinuses. (4) Nerve repair.

The following films were shown: (i) "Highspeed motion pictures of the human vocal cords" (Bell Telephone Labs.); (ii) "The Right to Hear" (State University of Iowa).

DISCUSSION ON FILM NO. I

Norman Patterson said since seeing this remarkable film he was more than ever convinced that the term vocal cord should be given up and some such substitute as vocal lip adopted. The structure in no way represented a cord and in the film transverse movements of a wave-like character could be seen which could not take place in a cord.

H. V. Forster said that whilst admiring these remarkable motion pictures of the vocal cords in action, he had been especially interested in the management of the laryngeal secretion.

The behaviour of the upper surface of the vocal cord gave the impression of "flag waving" with the sharp crest of a wave of the mucosa passing regularly from side to side. Distal to this crest there was being constantly maintained and controlled a shallow lake of fluid from which fine droplets appeared to be thrown at regular intervals over the wave crest to lubricate the glottic chink.

Remembering that one of the commonest words used by our patients to describe their symptoms was "catarrh", he felt that Colonel Canfield would agree that cinematography of such a high order offered an opportunity to study the behaviour of the laryngeal secretions in conditions of disease.

Lionel Collidge: I feel a particular appreciation of the film which Colonel Canfield has shown as I believe that Sir Charles Ballance and myself were the first to attempt to take moving pictures of the living larynx, and I have some understanding of the difficulties. The image of the larynx is apt to dance about over the field; this difficulty has been overcome and the image is kept well centred in the film shown. This is no doubt partly due to the very short exposure needed for the slow motion pictures, whereas we had to make much longer exposures to obtain a reasonable length of film. One point which the film displays is the difference in mechanism of the cords when the voice is produced in falsetto. McKenzie believed that there is a damping effect, which shortens the active portions of the cords like the strings of a violin, when the falsetto is produced, and the film shows clearly that this view is correct and that the mechanisms of production of tenor and falsetto are different. It is said that Braham, the leading tenor during the first half of the nineteenth century, had such perfect control of his voice that he was able to pass from the tenor to the falsetto without any break perceptible to his audience. Such capacity is very rare and the film explains why there is usually a break in passing from tenor to falsetto, especially noticeable in untrained voices. I think Mr. Norman Patterson has already won his battle, as I understand that vocal fold is now the accepted anatomical term, and I find that students fresh from the anatomical department now use it spontaneously instead of vocal cord.

Section of Otology

President—L. GRAHAM-BROWN, F.R.C.S.

[March 2, 1945]

Lesions of the Facial Nerve Due to War Injuries and Their Repair

By Major FRANK D. LATHROP, M.C., A.U.S.

Otolaryngologist, Lahey Clinic, Boston, Mass.

TRAUMATIC lesions of the facial nerve in its course through the temporal bone, neck and face constitute a small proportion of all wounds resulting from modern warfare and are of minor importance as a casualty figure. However, such injuries are of major concern to the recipient. The soldier afflicted with a complete peripheral facial paralysis often regards his disability as catastrophic and the constant facial asymmetry and the hideous distortion occurring on emotional stimulation are frequently of such a degree as to cause the individual to shun his fellow-men. Alterations in the sociologic, psychologic and economic status of such patients are not uncommon and justify every effort being made to rehabilitate the casualty without delay.

During the past seven months, 40 cases of facial nerve paralysis of the peripheral type, secondary to wounds received in the present war, have been encountered. The facial nerve has been explored in 27 of these patients in order to determine the nature of the injury to the nerve and to effect a repair whenever possible. The lesions presented in this series emphasize the complexity of the destructive processes wrought by both high and low velocity missiles with respect to the facial nerve and demonstrate that the anatomical restoration of the continuity of the facial nerve may be possible in the majority of cases.

Trauma to the facial nerve incurred as a result of battle wounds varies with the type of wounding agent and the location and extent of the wound. Fractures of the facial bones, mastoid process or skull are almost always present in such battle casualties and concurrent paralyses of the 2nd, 5th, 6th, 8th, 9th, 10th, 11th and 12th cranial nerves are not uncommon.

The location and extent of the wound are of significance in evaluating the injury sustained by the nerve. An extensive wound may present multiple areas of damage, the presence or absence of which can be ascertained only by careful search of the facial nerve in the path of the wound. In one case in this series the facial nerve presented a large neuroma at the level of the stylomastoid foramen, partial destruction of the cervical trunk and avulsion of the pes anserinus and adjoining branches. Gutter wounds of the temporal bone superior to the external auditory canal and those grazing the mastoid process produce a concussional type of palsy. In the present series these recovered spontaneously. Wounds involving the mastoid process at the level of the external auditory canal or below produce facial palsy as a result of contusion or destruction of a portion of the nerve. Penetrating or perforating wounds in which the point of entrance or exit is situated just anterior to the lobule of the ear offer a poor prognosis for reconstruction of the continuity of the facial nerve as the pes anserinus may be destroyed. Branches of the facial nerve, in its distribution to the facial muscles, are, on occasion, contused or severed by deep lacerations and result in partial paralysis of the face.

The nature of the agent producing the paralysis is of importance. While it has been impossible to obtain this information in each case due to the casualty's lack of definite knowledge regarding this point, sufficient data have been accumulated to permit an evaluation of the effect of blast and high and low velocity missiles upon the facial nerve.

Facial paralyses secondary to the blast of nearby explosives apparently are the result of an intraneural pathologic change produced by the pressure waves associated with such explosions, as in no case was a fracture of the temporal bone discernible by roentgenologic examination and spontaneous recovery occurred. Deafness and rupture of the tympanic membrane, as further evidence of the blast effect, was noted in each case.

High and low velocity missiles, on the other hand, are almost always associated with fractures of the temporal, mandibular or maxillary bones and cause paralysis as a result of concussion, compression, contusion or interruption of the nerve. There has been little difference noted between the amount of destruction caused by either of these two projectiles. The former produce either wounds of the perforating type with small entrance and exit points and extensive fracturing of the mastoid process, or large gutter wounds of the soft tissue and relatively slight disruption of the mastoid. The flat trajectory characterizing such missiles and causing roughly horizontally lying

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wounds tends to involve the vertical position of the facial nerve in the region of the stylomastoid foramen and the cervical trunk or its facial distribution. Injury to the facial nerve by low velocity missiles is almost always associated with extensive fracturing of the mastoid process. Such wounds are of the penetrating type and present wide destruction of the nerve. On occasion minute fragments may either enter the external auditory canal or pass between the stylomastoid foramen and the mastoid tip to either section or contuse the facial nerve.

The most significant feature of those wounds which resulted in interruption of the facial nerve is the magnitude of the loss sustained by the nerve. Exploration, on occasion, demonstrated the facial nerve to be either missing or so badly traumatized as to require excision from the region of the geniculate ganglion to within a few millimetres of the pes anserinus, a distance of approximately 65 mm. Losses involving a portion of both the mastoid and cervical segments are common. Infrequent, but offering an extremely poor prognosis for repair of the nerve, are those wounds which destroy the pes anserinus as well as its immediate branches. Avulsion of the facial nerve in its petrosal course is rare but did occur in one case. Interruptions of lesser magnitude do occur and are located usually in the cervical trunk or the distribution in the face.

Civilian experience would lead one to believe that radiography and electrical reactions and tests for taste and hearing would reveal if the nerve had been severed and also the approximate site of injury. However, in this series such examinations have been of relatively little practical value.

Taste testing has been unreliable in the majority of patients and has in all probability been due to the severe concussion which the nerve has sustained. Tests for the presence or absence of lacrimation have been more reliable. X-ray studies have been difficult to evaluate due either to failure of displacement of the fragments, in the presence of an existing fracture or to an inability to determine which fracture is producing the injury to the facial nerve. Faradic stimulation, however, has been of some value either in evaluating those paralyses secondary to concussion or in making the decision whether or not to explore a large wound in the vicinity of the parotid gland. Galvanic response has been elicited in every case tested.

The treatment of facial paralyses due to injury of the facial nerve at any point in its pathway through the temporal bone, neck or face incident to war wounds is surgical. That such surgery is justly the domain of the otologic surgeon should be without question. An exact knowledge of the anatomy of the facial nerve and the pathologic processes within the middle or inner ear with which such lesions are frequently associated are prerequisites for surgical intervention.

For restoration of function of the facial nerve operations such as decompression, end-to-end suture, nerve grafting or anastomosis of the distal stump of the facial nerve to the central end of an adjacent cranial nerve are successful in the majority of cases. Decompression is readily achieved following the accomplishment of either a simple or radical mastoidectomy as may be indicated by the pathologic process present. Exposure of the facial nerve within the fallopian canal is obtained by removing the postero-lateral bony canal wall on either side of the lesion until normal nerve tissue is observed and should be followed by slitting the sheath of the nerve. Compression by displaced fragments of bone, foreign bodies or œdema may be relieved in this manner.

Division of the facial nerve requires that the divided ends be freshened and the continuity restored whenever possible by end-to-end suturing or nerve grafting. When there has been but little loss of substance the junction may be obtained by mobilizing the distal segment in the neck and parotid gland and by exerting traction to gain about 6 mm. Greater losses can be overcome by re-routing the nerve should the pathologic process present permit a radical mastoidectomy. Gaps up to 23 mm. may be closed in this way.

Re-routing the facial nerve is a simple surgical procedure. A radical mastoidectomy is performed and the nerve uncovered sufficiently to permit lifting it out of the fallopian canal from the geniculate ganglion to the stylomastoid foramen. The cervical trunk of the facial nerve is liberated from the surrounding soft tissues and, if necessary, the dissection carried forward into the cheek so as to obtain greater mobilization of this portion of the nerve. Removal of the vaginal process of the temporal bone allows the nerve to be re-directed so that it courses from the geniculate ganglion vertically across the middle ear into the neck and permits end-to-end suture without tension (fig. 1).

If approximation of the divided ends cannot be accomplished by either of these methods, then recourse must be taken to nerve grafting in order to bridge the defect. For this purpose it is convenient to utilize the anterior femoral cutaneous nerve as the donor. The proximal and distal stumps of the facial nerve are carefully shaved until healthy nerve tissue is apparent and measures have been taken to insure a

bloodless operative field. A segment of the proper length is obtained from the donor nerve and inserted into the defect of the facial nerve so as to allow coaptation of the ends of the graft with those of the facial nerve. A nerve graft lying within the fallopian canal does not require suturing. However, in those cases in which the opposing ends lie in soft tissue, a single through-and-through suture of tantalum wire .003 of an inch in diameter is necessary in order to prevent separation.

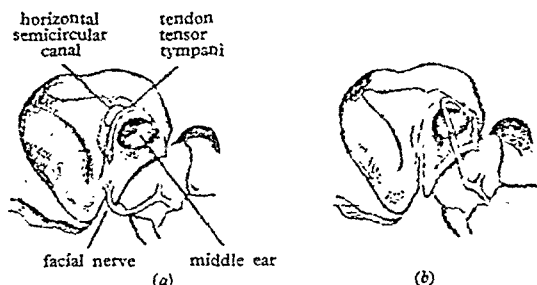


FIG. 1.—Re-routing of facial nerve: (a) Defect in facial nerve which would require nerve grafting if normal course of facial nerve was retained. (b) Defect closed and end-to-end suture accomplished by changing course of facial nerve. (Drawing by Sergt. Felix Weinberg, 192nd General Hospital, from an actual operated case.)

A single through-and-through stitch of fine tantalum wire has been used in this series whenever it was deemed necessary to maintain the neural junction rather than several perineural sutures. It is believed that better apposition of the nerve ends is obtained in this way and that trauma incident to the passing of several sutures through the perineurium is reduced to the minimum. Spurling [1] has demonstrated that tantalum is relatively inert in peripheral nerves and that this method of nerve suturing is practical.

Occasionally, the central end of the facial nerve is inaccessible, and as a last resort in such instances, anastomosis of the distal stump of the facial nerve with the central end of an adjacent motor nerve is essential. For this purpose the spinal accessory or hypoglossal nerves are admirably suited. Prolongation of the post-auricular incision downward into the neck along the anterior border of the sternocleidomastoid muscle permits exposure and mobilization of the central portion of either of these nerves. The peripheral end of the facial nerve is freed and the anastomosis effected and maintained by a single through-and-through tantalum wire suture. The descendens hypoglossi is sectioned and the proximal end sutured to the distal stump of the donor nerve in an effort to maintain tone in the muscles supplied by this nerve. Opinions vary as to whether the hypoglossal or spinal accessory nerve should be utilized for this surgical procedure, but as a general rule hypoglossal-facial anastomosis should be reserved for those individuals whose livelihood depends on manual labour while spino-facial anastomosis is desirable in those whose occupation is of a sedentary nature.

There still remains the rare case in which none of the above procedures is applicable and indwelling mechanical support must be supplied to obviate the unsightly deformity of the face. Total loss of the pes anserinus or inability to locate the severed branches of the facial nerve in its facial distribution are examples. Living mechanical support may be obtained by implantation of fascia lata. This is best accomplished by undermining the skin and immediate subcutaneous tissue over the entire affected side of the face through a hockey-stick incision over the temporalis muscle and threading strips of freshly obtained fascia lata through the deeper substance of the face by means of a suitable fascial needle in such a manner as to form three loops of fascia, one each running to the upper and lower lip and the third to the angle of the mouth. It is important that the fascial loops which are incorporated in the lips extend past the midline. The free ends of the fascial loops are adjusted and anchored within the temporalis muscle so as to cause over-correction of the facial deformity. Excess skin is excised, the incision closed and a pressure dressing applied to the face. An excellent cosmetic result when the face is in repose may be obtained with this method and slight animation of the paralysed face may occur when the temporalis muscle contracts.

Each of these methods of treatment was employed in this series as the pathologic process present indicated and the patient's condition permitted. Decompression was performed in seven cases. Laceration or contusion of the facial nerve had occurred within the middle ear in three of these patients, in the mastoid in another and in the facial distribution in the remaining three. Approximation of the distal and proximal ends of the interrupted facial nerve was accomplished in four instances. The cervical trunk was divided in two cases and a neuroma, secondary to a fracture passing through the stylo-

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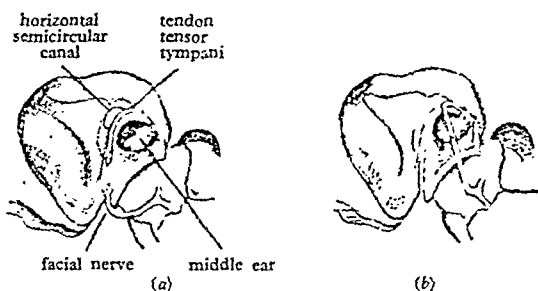


FIG. 1.—Re-routing of facial nerve: (a) Defect in facial nerve which would require nerve grafting if normal course of facial nerve was retained. (b) Defect closed and end-to-end suture accomplished by changing course of facial nerve. (Drawing by Sergt. Felix Weinberg, 192nd General Hospital, from an actual operated case.)

A single through-and-through stitch of fine tantalum wire has been used in this series whenever it was deemed necessary to maintain the neural junction rather than several perineural sutures. It is believed that better apposition of the nerve ends is obtained in this way and that trauma incident to the passing of several sutures through the perineurium is reduced to the minimum. Spurling [1] has demonstrated that tantalum is relatively inert in peripheral nerves and that this method of nerve suturing is practical.

Occasionally, the central end of the facial nerve is inaccessible, and as a last resort in such instances, anastomosis of the distal stump of the facial nerve with the central end of an adjacent motor nerve is essential. For this purpose the spinal accessory or hypoglossal nerves are admirably suited. Prolongation of the post-auricular incision downward into the neck along the anterior border of the sternocleidomastoid muscle permits exposure and mobilization of the central portion of either of these nerves. The peripheral end of the facial nerve is freed and the anastomosis effected and maintained by a single through-and-through tantalum wire suture. The descendens hypoglossi is sectioned and the proximal end sutured to the distal stump of the donor nerve in an effort to maintain tone in the muscles supplied by this nerve. Opinions vary as to whether the hypoglossal or spinal accessory nerve should be utilized for this surgical procedure, but as a general rule hypoglossal-facial anastomosis should be reserved for those individuals whose livelihood depends on manual labour while spino-facial anastomosis is desirable in those whose occupation is of a sedentary nature.

There still remains the rare case in which none of the above procedures is applicable and indwelling mechanical support must be supplied to obviate the unsightly deformity of the face. Total loss of the pes anserinus or inability to locate the severed branches of the facial nerve in its facial distribution are examples. Living mechanical support may be obtained by implantation of fascia lata. This is best accomplished by undermining the skin and immediate subcutaneous tissue over the entire affected side of the face through a hockey-stick incision over the temporalis muscle and threading strips of freshly obtained fascia lata through the deeper substance of the face by means of a suitable fascial needle in such a manner as to form three loops of fascia, one each running to the upper and lower lip and the third to the angle of the mouth. It is important that the fascial loops which are incorporated in the lips extend past the midline. The free ends of the fascial loops are adjusted and anchored within the temporalis muscle so as to cause over-correction of the facial deformity. Excess skin is excised, the incision closed and a pressure dressing applied to the face. An excellent cosmetic result when the face is in repose may be obtained with this method and slight animation of the paralysed face may occur when the temporalis muscle contracts.

Each of these methods of treatment was employed in this series as the pathologic process present indicated and the patient's condition permitted. Decompression was performed in seven cases. Laceration or contusion of the facial nerve had occurred within the middle ear in three of these patients, in the mastoid in another and in the facial distribution in the remaining three. Approximation of the distal and proximal ends of the interrupted facial nerve was accomplished in four instances. The cervical trunk was divided in two cases and a neuroma, secondary to a fracture passing through the stylo-

mastoid foramen, required excision in a third. The remaining patient exhibited division of two of the principal branches of the nerve in its facial distribution.

Restoration of the continuity of the divided nerve was obtained in nine cases by nerve grafting. Both fresh and pre-degenerated nerve grafts were utilized, the former on five occasions and the latter on four. The choice of a fresh or pre-degenerated graft was dependent upon the relative diameters of the facial and donor nerves. Thus, if the donor nerve was small it was crushed and allowed to degenerate for about two weeks so that the resultant increase in size of the peripheral portion would more closely approximate the diameter of the facial nerve. If, on the other hand, there was not too great a difference in the diameters, a fresh nerve graft was used.

Defects in the facial nerve ranging from 15 mm. to 50 mm. (the average being 33 mm.) were bridged in this manner. One graft of 15 mm. was utilized to repair a gap entirely confined to the cervical trunk of the facial nerve, while grafts of 26, 30, 30, 32 and 40 mm. were used to repair losses located both in the cervical and mastoid course of the nerve. In two patients, grafts of 45 and 50 mm. replaced missing segments of the facial nerve extending from the genu to the pes anserinus. The remaining case required a nerve graft of 30 mm. to restore the continuity of the facial nerve from immediately anterior to the horizontal semicircular canal to just distal to the stylomastoid foramen.

The facial nerve was absent in the petrosal, intratympanic and superior half of its mastoid course on one occasion. Repair was effected in this case by anastomosis between the distal stump of the facial nerve and the central end of the hypoglossal nerve. In two cases the pes anserinus and its immediate branches could not be found and the facial deformity was satisfactorily corrected in one by fascia lata implantation. The other, together with a patient in whom the facial nerve was absent from just anterior to the horizontal semicircular canal to, it is believed, the pes anserinus, had to be returned to the Zone of the Interior before further treatment of the facial paralysis could be effected. The continuity of the nerve could not be re-established in three instances in which the interruption of the facial nerve occurred in its facial distribution.

The care of the facial musculature is important in those cases in which it is anticipated that the facial paralysis will exist for a considerable period of time. Permanent sagging of the soft tissues and atrophy of the muscles will be reduced to the minimum if mechanical support and daily massage are instituted early. Support has been obtained in this series by adhesive traction or fascia lata slings. The latter method is desirable not only because it provides more natural support to the paralysed face, but also because permanent correction of the facial asymmetry is obtained in the event functional restoration of the facial nerve fails to occur.

Exploration of the facial nerve in these cases has proven to be especially difficult due to the loss of established anatomical landmarks in relationship to the nerve in its course through the temporal bone, and also, because of the displacement of the nerve within the soft tissues of the neck and face by the wounding agent. The surgeon operating on such cases must be thoroughly conversant with the anatomy of this region and be blessed with an infinite amount of patience and perseverance.

No attempt has been made to describe the results obtained in this series as insufficient time has elapsed to permit inclusion of those cases in which interruption of the facial nerve occurred. However, since restoration of the anatomical continuity of the nerve has been accomplished in most patients, it is believed, from previously reported experience with such grafts, that relief from the facial paralysis will be obtained which will be comparable to that encountered in civil life.

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Mr. Terence Cawthorne said that an account of 40 such cases was something new in their experience, and those who had attempted this kind of work would appreciate what

it meant to have done more than 20 cases over a short period of time. One question of interest was the introduction of sutures at the point of junction between the divided ends of the nerve. It had been found by Bentley and others that the introduction of suture material caused a certain amount of fibrosis however deftly it was done. It might be more desirable to use anchor sutures some distance away from the junction and to employ some such material as concentrated plasma solution for the actual join.

Brigadier M. L. Formby said that he himself had had no personal experience of dealing with these cases, but he had seen a number of them and had discussed them with the surgeons in charge. Where there was a severe lesion, involving the mastoid region, with considerable loss of facial nerve and tremendous scarring, it was extremely difficult to isolate the ends, and, having done so, to obtain a satisfactory result by grafting. Where the injury had been very severe he had been inclined to hand the case on to the plastic surgeon for restorative operations. Could Major Lathrop tell them definitely the result of his experiences in cases with extensive loss, whether he considered it justifiable to explore all cases, and whether he anticipated that a reasonable proportion would give satisfactory results? The other question was, what method did he use to protect his graft after he had put it in position?

Major Hoople, U.S.A.M.C., endorsed the remarks of other speakers to the effect that this work should not be entered upon lightly and that perseverance was necessary. What puzzled him was the distortion which occurred. The nerve on occasion was moved by as much as an inch from its supposed location, and to search for it in its usual position, with scar tissue, and not find it, would trouble the ordinary man. It would be of interest to them all if the procedure of grafting of the nerve were elicited a little more fully.

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The anatomical and pathological findings had been described in 27 of the 40 cases of facial paralysis in this series. The remaining 13 cases consisted of facial paralyses secondary to extensive lacerations of the face or cases in which it was considered inadvisable to operate because of associated wounds of greater importance.

Major Lathrop was in agreement with Mr. Cawthorne with respect to the difficulty of operating on these patients with facial paralysis secondary to war wounds. Facility in the operative technique increased with experience and decreased the operating time. In general, such operations were lengthy and it was not uncommon to operate four or five hours only to reach such a stage in the operation as to permit completion of the surgical repair of the facial nerve at another time.

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Considerable difficulty in locating the proximal and distal ends of the facial nerve was encountered in these cases of facial paralysis secondary to war wounds because of

the extreme distortion present. It was a relatively simple matter to perform the necessary bone work on the mastoid process but, as a result of the large amount of granulation tissue present in the wound if two or three weeks had elapsed since it was incurred, considerable difficulty was experienced in locating the ends of the facial nerve. In such instances it was necessary to "pick up" the facial nerve at a point external to the wound, in so far as this was possible, as the relationship of the facial nerve to the existing anatomical landmarks was less likely to be disturbed. The greatest difficulty was experienced in locating the distal end of the nerve. Frequently the pes anserinus was displaced by the wounding agent and thus might lie either inferior, superior or superficial to its normal position. As a general rule, it was necessary to spend the best part of an hour in discovering the distal segment of the facial nerve.

The postoperative care was simple. In the past it had been the practice of the pioneers in the surgical treatment of facial paralysis to cover the nerve graft with gold leaf. However, he believed that this procedure had since been abandoned. It had been his custom to cover the graft in the facial nerve, when it lay in the mastoid cavity, with a piece of sterile cellophane which in turn is covered with lightly packed vaseline iodoform gauze. The gauze packing and the cellophane are removed at the end of a week. Some difficulty might be experienced in locating and removing the cellophane since it was transparent. At this time the mastoid cavity was usually found to be lined with granulation tissue and the nerve graft cannot be observed although, at times, a thin reddish streak might be noted where the graft should exist. In the event that the nerve graft was located in the soft tissues of the neck it was not covered with cellophane as the soft tissues afford sufficient protection.

It was difficult to answer the question as to whether the facial nerve should be explored in every case of facial paralysis secondary to war wounds. It would seem, if one was reasonably certain that the facial nerve had been sectioned, that exploration of the facial nerve was the only logical way in which to determine definitely whether such was the case or not. An endeavour should be made to effect restoration of the continuity of the nerve whenever possible.

The question was asked by Mr. Thacker Neville as to how stretching of the facial musculature was prevented. It has been the writer's practice in the most recent cases to thread strips of fascia lata through a "hockey-stick" incision over the temporalis muscle on the same side as the facial paralysis, from the upper and lower lips as well as from the angle of the mouth to the temporalis muscle by means of a long, large-bore, steel needle incorporating a loop of steel or brass wire, as had been demonstrated on the blackboard. This procedure took about an hour to perform and gave rise to very little reaction and an excellent cosmetic and supportive result.

In conclusion, Major Lathrop said that he did not believe that any of these operative procedures should be attempted by the beginner. The initiate should act as an assistant until he was thoroughly familiar with the anatomy of the region and the variations encountered. Fortunately, most of these cases were "clean" but he did not believe that the presence of a low grade infection was a serious deterrent whenever it was found necessary to use a nerve graft in order to effect the anatomical continuity of the facial nerve.

Section of Otology with Section of Laryngology

COMBINED SUMMER MEETING HELD IN LONDON

[June 1, 1945]

OTOLOGICAL SESSION

Chairman—L. GRAHAM BROWN, F.R.C.S.

(President of the Section of Otology)

Demonstration of R.A.F. Hearing Tests

By Air Commodore E. D. D. DICKSON

THE work of devising new hearing tests to be applied to aviation candidates has been carried out in the Ear and Throat Department and Acoustics Laboratory at the Central Medical Establishment by a team of clinical and scientific investigators (*Proc. R. Soc. Med.*, 1943, 36, 398). The tests have been applied to Service airmen candidates and we are satisfied that they are a means of selecting the best material for the demands of present-day flying.

The method in present use for assessing the hearing ability of aviation candidates consists in testing the candidate's ability to hear the whispered voice with each ear separately when he is at a standard distance of 20 ft. from the speaker. The candidate fails the test, and is consequently debarred from all flying duty if he requires to be less than 20 ft. from the speaker in order to recognize correctly the isolated words which are whispered to him. The test is in fact a gross form of threshold test of speech, and

is used only to detect in a rough and ready fashion the presence of a hearing defect in either of the candidate's ears. It is doubtful if it can give a reliable indication of the serviceability of the candidate's hearing for the work he will have to do if accepted for air-crew duties and while the present test is in force a number of candidates are being rejected for flying duties who would, in fact, be quite capable of performing those duties: this constitutes the chief objection to the present method.

The other weaknesses of the present test lie in the lack of standardized testing conditions. The test is applied by a large number of medical officers at various centres. There are differences in the technique of the medical officers who give the test, involving differences in the quality and intensity of the whisper which is used.

The listening conditions too at examining centres vary quite widely. Rooms of different sizes, shapes and materials are used and varying amounts of ambient noise may be present when the candidate is tested; in some centres there is always a high level of background noise, in others a reasonably low level, and in the majority the noise level fluctuates considerably throughout the day. Again the speech material used for the test is not well controlled. In some cases the medical officer has a small selection of words which he uses on every candidate. These words soon become known by the men who come up for the medical examinations and it is quite possible for a candidate to pass the examination if he can pick up only a very small fraction of the signal which is whispered to him since he is in the position of knowing what to expect. Again there is no fixed policy as to the type of word to be used, nor as to what constitutes the passing of the test. In some centres men are tested with words containing some a preponderance of high-frequency and others of low-frequency components and they may be failed, for example, if they cannot hear the high-frequency words at 20 ft. At other places candidates are passed because they can hear some of the words at 20 ft. Whilst these inconsistencies have little importance for the vast majority of candidates who have "normal" hearing and are capable of passing the test under almost every condition, they are important for the borderline cases who might be failed at one examining centre but would be passed at another.

The new tests which we have devised fulfil two primary requirements. They constitute a measure of the candidate's hearing ability when working in real life conditions and they are applied in strictly standardized conditions so that the results from different examining centres are comparable.

Flying conditions impose certain limitations in communication. In the first place signals have always to be delivered through electrical channels terminating in some transducing unit. Secondly, the presence of the high level of ambient noise in aircraft makes it necessary to work with audible signals of considerable intensity. Even when signals are what is normally described as "faint", their absolute level is always considerably above threshold in quiet. Thus the type of hearing ability which is really required of air-crew personnel is the ability to hear signals well above threshold but in an unfavourable signal/noise ratio. No attempt has ever been made to correlate this ability with the ability to hear the whispered voice at given distances. It is unlikely that a complete correlation would appear between these two quantities since it is well known that there are types of deafness in which the hearing defect is apparent only for sounds near threshold, i.e. the hearing at some supra-liminal intensity is equal to normal and other types which for masking noise of a particular character will convert an unfavourable signal/noise ratio into quite a reasonable one. A level of background noise approximating 120 phons. is not uncommon, and we have to ensure that a man can receive signals satisfactorily in these conditions. Testing by any kind of threshold method of pure tones apart from the difficulties attendant upon such testing will not tell us the whole story. Ability to interpret signals depends on both hearing and intelligence, coupled with training. The new tests we present consist of two parts:

(a) An articulation or efficiency test which tests the candidate's ability to interpret speech in a background of noise; this is a binaural test.

(b) A diagnostic test as a means of screening individuals who may suffer from a hearing defect in one or both ears. This tests each ear separately, which is necessary since some people who pass the efficiency test may have defective hearing as proved by pure-tone audiometry.

It is important to be able to pick out such cases for two reasons: (i) The defect may be symptomatic of a condition which is likely to deteriorate more or less rapidly and therefore it might be inadvisable to take such a man into the Service; (ii) when cases of compensation or "pension" for hearing disability have to be decided it is essential to know the state of a man's hearing when he entered the Service.

The only really satisfactory test for this purpose is individual pure-tone audiometry but for a variety of reasons this method is impracticable and not acceptable to the Service.

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the extreme distortion present. It was a relatively simple matter to perform the necessary bone work on the mastoid process but, as a result of the large amount of granulation tissue present in the wound if two or three weeks had elapsed since it was incurred, considerable difficulty was experienced in locating the ends of the facial nerve. In such instances it was necessary to "pick up" the facial nerve at a point external to the wound, in so far as this was possible, as the relationship of the facial nerve to the existing anatomical landmarks was less likely to be disturbed. The greatest difficulty was experienced in locating the distal end of the nerve. Frequently the pes anserinus was displaced by the wounding agent and thus might lie either inferior, superior or superficial to its normal position. As a general rule, it was necessary to spend the best part of an hour in discovering the distal segment of the facial nerve.

The postoperative care was simple. In the past it had been the practice of the pioneers in the surgical treatment of facial paralysis to cover the nerve graft with gold leaf. However, he believed that this procedure had since been abandoned. It had been his custom to cover the graft in the facial nerve, when it lay in the mastoid cavity, with a piece of sterile cellophane which in turn is covered with lightly packed vaseline iodoform gauze. The gauze packing and the cellophane are removed at the end of a week. Some difficulty might be experienced in locating and removing the cellophane since it was transparent. At this time the mastoid cavity was usually found to be lined with granulation tissue and the nerve graft cannot be observed although, at times, a thin reddish streak might be noted where the graft should exist. In the event that the nerve graft was located in the soft tissues of the neck it was not covered with cellophane as the soft tissues afford sufficient protection.

It was difficult to answer the question as to whether the facial nerve should be explored in every case of facial paralysis secondary to war wounds. It would seem, if one was reasonably certain that the facial nerve had been sectioned, that exploration of the facial nerve was the only logical way in which to determine definitely whether such was the case or not. An endeavour should be made to effect restoration of the continuity of the nerve whenever possible.

The question was asked by Mr. Thacker Neville as to how stretching of the facial musculature was prevented. It has been the writer's practice in the most recent cases to thread strips of fascia lata through a "hockey-stick" incision over the temporalis muscle on the same side as the facial paralysis, from the upper and lower lips as well as from the angle of the mouth to the temporalis muscle by means of a long, large-bore, steel needle incorporating a loop of steel or brass wire, as had been demonstrated on the blackboard. This procedure took about an hour to perform and gave rise to very little reaction and an excellent cosmetic and supportive result.

In conclusion, Major Lathrop said that he did not believe that any of these operative procedures should be attempted by the beginner. The initiate should act as an assistant until he was thoroughly familiar with the anatomy of the region and the variations encountered. Fortunately, most of these cases were "clean" but he did not believe that the presence of a low grade infection was a serious deterrent whenever it was found necessary to use a nerve graft in order to effect the anatomical continuity of the facial nerve.

Section of Otology with Section of Laryngology

COMBINED SUMMER MEETING HELD IN LONDON

[June 1, 1945]

OTOLOGICAL SESSION

Chairman—L. GRAHAM BROWN, F.R.C.S.

(President of the Section of Otology)

Demonstration of R.A.F. Hearing Tests

By Air Commodore E. D. D. DICKSON

THE work of devising new hearing tests to be applied to aviation candidates has been carried out in the Ear and Throat Department and Acoustics Laboratory at the Central Medical Establishment by a team of clinical and scientific investigators (*Proc. R. Soc. Med.*, 1943, 36, 398). The tests have been applied to Service airmen candidates and we are satisfied that they are a means of selecting the best material for the demands of present-day flying.

The method in present use for assessing the hearing ability of aviation candidates consists in testing the candidate's ability to hear the whispered voice with each ear separately when he is at a standard distance of 20 ft. from the speaker. The candidate fails the test, and is consequently debarred from all flying duty if he requires to be less than 20 ft. from the speaker in order to recognize correctly the isolated words which are whispered to him. The test is in fact a gross form of threshold test of speech, and

is used only to detect in a rough and ready fashion the presence of a hearing defect in either of the candidate's ears. It is doubtful if it can give a reliable indication of the serviceability of the candidate's hearing for the work he will have to do if accepted for air-crew duties and while the present test is in force a number of candidates are being rejected for flying duties who would, in fact, be quite capable of performing those duties: this constitutes the chief objection to the present method.

The other weaknesses of the present test lie in the lack of standardized testing conditions. The test is applied by a large number of medical officers at various centres. There are differences in the technique of the medical officers who give the test, involving differences in the quality and intensity of the whisper which is used.

The listening conditions too at examining centres vary quite widely. Rooms of different sizes, shapes and materials are used and varying amounts of ambient noise may be present when the candidate is tested; in some centres there is always a high level of background noise, in others a reasonably low level, and in the majority the noise level fluctuates considerably throughout the day. Again the speech material used for the test is not well controlled. In some cases the medical officer has a small selection of words which he uses on every candidate. These words soon become known by the men who come up for the medical examinations and it is quite possible for a candidate to pass the examination if he can pick up only a very small fraction of the signal which is whispered to him since he is in the position of knowing what to expect. Again there is no fixed policy as to the type of word to be used, nor as to what constitutes the passing of the test. In some centres men are tested with words containing some a preponderance of high-frequency and others of low-frequency components and they may be failed, for example, if they cannot hear the high-frequency words at 20 ft. At other places candidates are passed because they can hear some of the words at 20 ft. Whilst these inconsistencies have little importance for the vast majority of candidates who have "normal" hearing and are capable of passing the test under almost every condition, they are important for the borderline cases who might be failed at one examining centre but would be passed at another.

The new tests which we have devised fulfil two primary requirements. They constitute a measure of the candidate's hearing ability when working in real life conditions and they are applied in strictly standardized conditions so that the results from different examining centres are comparable.

Flying conditions impose certain limitations in communication. In the first place signals have always to be delivered through electrical channels terminating in some transducing unit. Secondly, the presence of the high level of ambient noise in aircraft makes it necessary to work with audible signals of considerable intensity. Even when signals are what is normally described as "faint", their absolute level is always considerably above threshold in quiet. Thus the type of hearing ability which is really required of air-crew personnel is the ability to hear signals well above threshold but in an unfavourable signal/noise ratio. No attempt has ever been made to correlate this ability with the ability to hear the whispered voice at given distances. It is unlikely that a complete correlation would appear between these two quantities since it is well known that there are types of deafness in which the hearing defect is apparent only for sounds near threshold, i.e. the hearing at some supra-liminal intensity is equal to normal and other types which for masking noise of a particular character will convert an unfavourable signal/noise ratio into quite a reasonable one. A level of background noise approximating 120 phons. is not uncommon, and we have to ensure that a man can receive signals satisfactorily in these conditions. Testing by any kind of threshold method of pure tones apart from the difficulties attendant upon such testing will not tell us the whole story. Ability to interpret signals depends on both hearing and intelligence, coupled with training. The new tests we present consist of two parts:

- (a) An articulation or efficiency test which tests the candidate's ability to interpret speech in a background of noise; this is a binaural test.
- (b) A diagnostic test as a means of screening individuals who may suffer from a hearing defect in one or both ears. This tests each ear separately, which is necessary since some people who pass the efficiency test may have defective hearing as proved by pure-tone audiometry.

It is important to be able to pick out such cases for two reasons: (i) The defect may be symptomatic of a condition which is likely to deteriorate more or less rapidly and therefore it might be inadvisable to take such a man into the Service; (ii) when cases of compensation or "pension" for hearing disability have to be decided it is essential to know the state of a man's hearing when he entered the Service.

The only really satisfactory test for this purpose is individual pure-tone audiometry but for a variety of reasons this method is impracticable and not acceptable to the Service.

Our new test answers two questions: (1) Is the candidate deaf in one or both ears? (2)

Will he be able to do his job as an air-crew member efficiently—i.e. as far as hearing ability goes? An affirmative answer to the first question does not mean inevitably a negative to the second, or vice versa.

To Squadron Leader Fry and to the Technical Staff of the Laboratory the test owes much.

Squadron Leader D. B. Fry: On the last occasion when we addressed the Section we gave a full account of the theoretical principles which underlay our work (*Proc. R. Soc. Med.*, 1943, 36, 401).

The object of these hearing tests is twofold: first, we wish to discover whether a candidate is likely to be efficient as a member of air crew from the point of view of hearing, and, second, we want to find out whether the candidate suffers from any hearing loss which would make him unacceptable from the clinical point of view. These two tasks are not identical. A man's performance at threshold is not a reliable indication of his performance at supra-liminal intensities. I think it is logical, but it is perhaps a rather new idea, to believe that the pure tone audiogram does not tell the whole story. The kind of ability we want to measure in an air-crew candidate—the ability to work in a noise field of something like 110 decibels—requires that he should hear and understand very loud signals in a very loud noise. When we want to measure his threshold, we ask him whether he can hear a very soft signal with no masking noise at all. It is obvious that the two functions are not identical.

That is the reason why this hearing test contains two parts, one designed to give a rough form of pure-tone audiogram and the other to indicate whether a particular candidate is likely to be able to work in a loud noise and to receive speech signals of high intensity, in such a noise.

Machines used in applying the tests.—One of the chief requirements for the tests was that we should be able to deliver certain signals to a large number of candidates and be sure that every candidate received signals which were the same in frequency content and intensity. The simplest way of insuring this was by a gramophone and the machines which we use for carrying out the tests are nothing more than electrical gramophones of a particular design constructed in the Acoustics Laboratory on a model designed by Flying Officer R. E. C. Brown. Each machine feeds ten pairs of telephones and therefore one can test ten men at the same time. The switching arrangement makes it possible to send the signals into any single telephone in the ten pairs. We have tried to make the signal channels in these gramophones of as high fidelity as possible; the amplifier has a good frequency characteristic and we have used earpieces which give quite good results. All the signals which are used for both tests come from gramophone discs.

The first test consists in sending to the candidate a series of pure-tone signals and testing his ability to hear those signals at a low intensity. We have adopted an intensity level of 20 decibels above threshold as our standard. That figure has been accepted largely by otologists as representing normal hearing. By that I mean that although a person with no hearing defect would be expected to hear signals at an intensity lower than 20 decibels, on the other hand there are likely to be variations in the threshold of the same person from day to day and it is generally accepted that hearing losses up to 20 decibels are not indicative of an established hearing defect.

Five frequencies are used, 250, 500, 900, 2,000 and 4,000 cycles per second and the signals at each frequency are sent out at 20 decibels above threshold. In order to test a candidate's response we use a system of pips, similar to those used in the radio time signal. The pips are arranged in groups, each consisting of 3 or 4 pips. We begin the test with the 4,000 cycle signals and the announcement is made to the candidate that he is going to hear the set of signals which is identified as Number 1. He then hears three groups of pips, counts them and writes down the numbers that he hears; his response might be, for example, 333 or 434. The form on which the responses are written is so arranged that this becomes a very simple procedure. Two further sets of signals are given at 4,000 cycles and then the frequency changes to 2,000 cycles. Three sets of signals are given at this and at each of the other test frequencies. The first set of groups at each frequency is used to accustom the candidate to the new pitch and the response to this set is disregarded when the test is marked, though naturally the candidate is given no hint that this is so. In order to pass the test at a given frequency he must get two out of three groups correct in both the second and third sets of signals.

In this test the candidate uses one ear at a time. When he has completed the test for the two ears, we are able to determine whether he has any loss greater than 20 decibels in either ear.

It is evident that this is a very gross form of hearing threshold test, but we have found it to be satisfactory within its limitations. A large number of candidates have been examined by this method and by individual pure-tone audiometry. When individual audiometry is treated as a pass-fail test with 20 decibels as the pass level, the agreement between the two methods of testing is very good indeed.

The other part of the test is intended to determine whether the candidate is likely to be able to work in a loud noise and whether he can understand speech signals when they arrive in the presence of such a noise. In its final form the test consists in sending to the candidate signals in the form of common English single-syllable words. The speech arrives in the listener's telephones mixed with a very loud masking noise which is a fairly good representation of what a man hears when he is flying and is wearing a helmet. The intensity level of the masking noise is about 100 decibels and the peaks of the speech are about 106 decibels, so the signal to noise ratio is not very favourable.

As to the linguistic material used in the test, the word lists were made up in the laboratory on certain principles. We undertook a count of speech sounds in current English speech and also carried out experiments to determine which sounds were most frequently mistaken when they were heard against a background of masking noise. Values for the percentage frequency of occurrence and the percentage frequency of error were calculated for each sound and these two values were combined by taking their product. The speech sounds were arranged in order of the magnitude of this product and the sounds which occurred most frequently and were most frequently mistaken were

used in making up the test words. The sounds were combined into single-syllable words and these words were made up into lists in such a way that the sound distribution in each test list should be very close to that of normal English speech. In point of fact we had to omit altogether one or two sounds because we knew that the electrical channels would be incapable of reproducing the distinctions between them. If we take, for example, the words *thin* and *fin*, even the highest fidelity channel will not reproduce the difference between the first sounds in these words with a certainty of 100%. It was obviously pointless to include distinctions of that sort in our test when we knew that the system was incapable of passing them. Apart from this reservation, all the test lists were made up on the lines I have indicated.

Two lists, each consisting of forty words, are used in the complete test. The first six words in each list are disregarded in marking (though we do not tell the candidates this); they allow time for the listeners to get used to the masking noise, to the speaker's voice and to writing down the words. The test is based entirely on the principle of sounds right or wrong, not on words right or wrong. For example, the word *sock* would carry three marks, one for the initial, one for the vowel and one for the final consonant, and if the candidate gets any part of the word correct he gains credit for it. If he wrote the word as *sob* he would score two marks, if he wrote it as *sack* he would again receive two marks, if he wrote *tack* he would get only one mark. Candidates are instructed to write down any part of a word which they hear; for example, if they hear a word beginning with *t*, without hearing the rest of the word, they should write *t*—in order to gain credit for hearing this sound. If a candidate's rendering of the word *sock* were *stock*, he would still be allowed three marks because a sound is marked right provided it is in the right position, even though other sounds are added. We have found that this is a good way of achieving consistent marking.

[The members of the Sections then had their hearing tested in the way described.]

In reply to questions, Squadron Leader Fry said that 20 decibels was a fairly low level and perhaps a few of those present would know already that they had a hearing loss at 4,000 cycles which exceeded this value. He had seen one "candidate", a member of the Section, who had been unable to record anything until the fourth set of signals, which meant that he was unable to hear those at 4,000 cycles at all. The candidates for the R.A.F. were usually between the ages of 18 and 21 and one would not expect a great many of them to have a hearing loss for 4,000 cycles. There seemed, therefore, to be no grave objection to beginning the test with the high-frequency signals.

He did not know of any method so far devised which was likely to supersede pure-tone audiometry as a quantitative test of hearing. Tuning forks were used as a clinical test but not as a quantitative one.

The masking noise was certainly rather high and the speech somewhat low in intensity. On the other hand, the quality of the speech was better than that heard from aircraft intercommunication equipment. The difference between the accent of the speaker on the disc and that of the listener was important and it was for that very reason that every candidate was asked to state his nationality. When the responses to the test were marked, certain allowances were made for differences of accent. In the test word *heart*, for example, in southern English pronunciation most speakers used no "r" sound and so the word became *h-vowel-t*. Some American candidates wrote down the word as *hot* because that coincided with their pronunciation and this response would be counted correct for such a candidate.

The numbers were much easier to understand than the test words because the listener knew what to expect before the number was pronounced. One anticipated that "number three" would follow "number two" and therefore "number three" was understood without any trouble, whereas the test word was something which could not possibly be predicted. Because of this, the impression was gained that the test word was actually louder than the number, but there was in fact no difference in intensity level between the numbers and the test words. The same was true of the opening announcement of the test.

While listening to the test one did not actually listen to the numbers and it was found in practice that it did not matter whether there were a pause or not between the announcement of the number and the saying of the test word since the number served only as a warning.

An 8,000 cycle note would be impossible to reproduce from the gramophone disc at the required level. The system was not sensitive enough at those frequencies to give a satisfactory signal and that, combined with the length of the test, was the practical reason why it had not been possible to include 8,000 cycles in the test. But given the particular purpose of the test it seemed in any case scarcely necessary to include this frequency. The signals heard from the gramophone disc had been taken originally from a group pure-tone audiometer which had been developed for use by the Air Ministry but which had not been taken up to any great extent.

Concerning the words used in the efficiency test, there were differences between the lists recorded on the disc and those used by the late Dr. Kerridge. In the latter, the words might contain consonant clusters, as for example in the word *spring*, but in the lists now in use, in order to simplify the system of marking, no word contained more than consonant-vowel-consonant. Short signals had been used in the pure-tone test because it was so difficult to get from the gramophone a signal which was constant in frequency. The pips were evidently not quite short enough since some of those who had been tested that morning had detected that there was a change of frequency within each pip.

Colonel Canfield, U.S.A.M.C., said that he had had the opportunity of following this work for two and a half years and he believed it to be a magnificent contribution to the testing of large groups of candidates for any particular job. He had already recommended to his authorities at home that a hearing test should be done on discharged soldiers, and it was hoped to obtain some useful figures. It would be interesting to know whether, after this test had been used for some time, the men admitted to the Royal Air Force on the strength of the test had turned out to be as satisfactory as was thought. Squadron Leader Fry, in answer to a question on the marking of the test, said that

Will he be able to do his job as an air-crew member efficiently—i.e. as far as hearing ability goes? An affirmative answer to the first question does not mean inevitably a negative to the second, or vice versa.

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Section of Odontology

President—H. T. ROPER-HALL, M.B., M.D.S.

[April 30, 1945]

Cervico-Facial Actinomycosis. [Abridged]

By ALEXANDER B. MACGREGOR, M.A., M.D., B.Chir.Cantab.,
M. and L.D.S. R.C.S.Eng., S/Ldr., R.A.F.V.R.

Ætiology.—The disease was first described in cattle by Bollinger in 1877 and in man by Ponfick in 1879, but the first detailed clinical description of the disease in man was given by J. Israel in 1885.

For years a tradition has grown up that grooms and other workers associated with cattle or horses were more liable to the disease than others, and the fact that similar-looking organisms could be found on grasses and straw gave further credence to this view. But Erikson (1940) has shown that there are marked differences both morphological, and in reaction, between the bovine and human strains, and the aerobic organisms present on vegetation are non-pathogenic to both animals and man.

It has further been shown by Lord (1933), Naeslund (1925) and Emmons (1935) that anaerobic strains corresponding morphologically and culturally to the pathological human *A. israeli* type can be found in normal mouths.

It seems probable therefore that under certain circumstances, e.g. trauma, the organisms normally saprophytic in the mouth become parasitic and the disease manifests itself. This view is supported by the almost invariable history of trauma, e.g. extraction of a tooth or fracture of the mandible, which precedes the onset of the disease.

The organism spreads along cellular planes or by the blood-stream, and involvement of lymph nodes is usually due to the presence of secondary infection. It is one of the more curious features of the disease that an organism that apparently gains entrance in many cases through a tooth socket, should cause abscesses in the cervico-facial region leaving no sequelæ in the original area of the portal of entry. Bone involvement is rare.

Incidence.—It is probable that in a great many cases the condition is not recognized, since careful examination and anaerobic culture of the pus from cervical abscesses are often not undertaken. Patients may present with a single abscess, e.g. fig. 1, under the chin or on the neck and the classical form with multiple sinuses is not necessarily seen.

In the present series of ten patients, six started with single abscesses only, though bacteriological examinations showed the presence of true actinomycosis in these as well as the remaining four. In only one case was there obvious bone involvement.

Treatment.—Iodine and X-ray therapy have in the past been the most widely used methods of treatment. In the present series iodine has not been used and X-rays have been used on only two patients without any outstanding success. Excision of the whole area in one very localized case has been performed without recurrence of the disease. One case with a submental abscess following fracture of the mandible has been treated by drainage alone, and although the abscess contained undoubted actinomycotic pus from which the organism was grown, there has been no recurrence over a period of one year. Two patients have been treated with a suspension of sulfa drugs injected into

the test was based on the principle of one mark for each correct sound. On each disc there were 100 sounds and by counting up the number the candidate had got right one arrived at a percentage for each half of the test. The pass mark at present was 60%, that is if a candidate got 120 out of the 200 sounds right he was considered satisfactory.

Concerning the validation of the efficiency test of which Colonel Canfield had spoken, this was a very difficult matter. They had tested 7,000 candidates with these machines since last August, and of those 7,000 not one had yet completed his flying training. At this distance of time it could not be stated whether any single one of these men was satisfactory as a member of air crew. He very much doubted whether even in the end figures could be placed before them to prove that the test was absolutely valid. One could only say that if the battery of tests were applied to a large number of people, it was probable that a better selection of men would be obtained by this than by any other criterion. When they had used the efficiency test in the otological department, they had always found that the men who were returned to the department because they were unable to hear intercommunication signals had invariably done badly in this test. On the other hand, those who were supposed to be satisfactory as members of air crew had always passed the test. He thought it must be taken logically that this combination of tests was going to give a better selection of candidates.

In reply to another question, he said that a certain degree of hearing loss might actually be an advantage to someone who had to work in a loud noise. A man with a low tone loss of not too marked a degree was likely to do well in the efficiency test because his low tone loss reduced the masking effect of the background noise.

Asked whether it was possible to discover any relationship between the result of the efficiency test and the results of a general intelligence test, Squadron Leader Fry said that at one time, early in their experiments, they had certainly tried to find a correlation between a man's performance in the hearing efficiency test and his performance in general intelligence tests. They were able to take only a sample of 100 men, and in this sample they were unable to discover any close correlation. General intelligence was obviously quite an important factor in the skill that was being measured but as they could not prove the required correlation they were compelled to continue the development of the specialized hearing efficiency test.

He also said that men who failed in the 20 ft. whisper test would not necessarily fail in the efficiency test and vice versa. Each of the tests would reject a slightly different group of men.

In reply to further questions, he said that he hoped those present would not be misled by the fact that their domestic jargon had labelled this a pure-tone disc. They did not set out to produce something which would replace a pure-tone audiometer. They did not imagine that the signals produced from the gramophone disc were in reality pure tones and they knew that stimulation by broken signals was different from stimulation by a continuous signal, but what they set out to do was to find some method of testing, the results of which would correlate quite closely with those of pure-tone audiometry and the criterion of the success or failure of the test was the degree of this correlation.

In using articulation tests, two alternative methods were possible. One could either arrange a test in which all the speech sounds occurred with the same frequency as in normal speech, or, on the other hand, one in which all sounds occurred an equal number of times. If the second method were adopted, a weighting process had to be carried out in calculating the results of the test. The test which they had devised employed the first method; the weighting was already done in the distribution of the sounds throughout the test. He had been asked about the value of nonsense syllables. He thought that in this case a nonsense syllable test was not practicable. A candidate was under test for only twenty minutes; he could be tested only once and it was not possible to carry out any nonsense syllable test unless the listener had been trained in some way to write down what he heard. He agreed that the nonsense syllable method was a good one if one wanted to establish the articulation of a particular system, but it could only be carried out if there were a chance of training the personnel in recording their responses to the test and that was out of the question in the work of air-crew medical boards.

He had also been asked about fatigue. They had no very definite evidence on this subject; they were content for the moment to decide whether a man was likely to perform efficiently, but of course it would be a very good thing if one could eliminate candidates who were easily fatigued by noise. Such cases did exist and were occasionally returned to the Central Medical Establishment.

Asked about the wearing out of the wax records, he said that experiments had been carried out to demonstrate the change of articulation score with the use of a new or an old disc. In the experiment, they compared the performance on a new disc with that on a disc which had been played fifty times. The change in the mean score was very small indeed—something of the order of 2% lower in the case of the worn disc. They took this as an indication that it is wiser not to use a disc fifty times and accordingly they had limited the life of the disc to thirty playings. A similar experiment had been carried out with the reproducing needle.

Air Commodore Dickson, in reply to a question, said that Wing Commander Bateman and himself were shortly publishing a paper giving the details of their findings. They had not found that the whisper test as applied outside had been a satisfactory one from the point of view of selecting the right people for flying duties.

Mr. G. Ewart Martin asked whether the R.A.F. had had the opportunity of examining some of these candidates not once but two or three times. He did not suppose that the tuning fork had been used in conjunction with these tests for low tones only.

Wing Commander Bateman replied that the early otosclerotic detected by tuning fork would not have passed the pure-tone test. The tests had not yet been accepted as the official R.A.F. standard of hearing for acceptance of air crew and so there had been no opportunity of retesting large numbers of men. He thought it would be found when this test did come into operation that it would eliminate the otosclerotics, whereas they did pass the whisper test without difficulty. The negative Rinne did not appear usually until there had been a loss on the pure-tone audiometer of more than 20 db., at the level tested by the tuning fork.

The Recuperative Power of the Dental Pulp

By LILIAN LINDSAY, M.D.S.Durh., L.D.S.Edin.

AMONG the more interesting specimens shown by Sir Frank Colyer from the Odontological Museum of the Royal College of Surgeons was that of the recovery of the dental pulp after severe injury to the tusk of an elephant. Comparison of Sir Frank's reasoning, supported by sections of the tusk, as to the stages of recovery from chaos to the ordinary ivory of commerce, with similar conditions in the human pulp, has never been attempted so far as I am aware. The reported cases, illustrated by microscopical sections, are so few that, except for a description in Hopewell-Smith and illustrations in textbooks such as Tomes and Colyer and Sprawson, little reference has been made to the remarkable recuperative power of the human pulp seen in these specimens.

Their bearing upon traumatic exposure deserves attention, especially in the recent light thrown by Manley upon the biology and histopathology of the pulp. The effect of filling materials upon the pulp would seem, at first sight, to have little connexion with traumatic exposure, but careful and more concentrated attention and comparison of the healing of gross injury in septic surroundings with failure to heal slight injury treated with every aseptic and antiseptic precaution, reveals some points of an interesting nature.

Why should an injury which would be regarded as a compound fracture in the rest of the body, heal, and the tissues concerned regenerate, when a slight injury such as traumatic exposure treated with all the care known to dental practice end in the death of the pulp? Is it an example of the old adage "Killed by kindness"?

Watson Cheyne, speaking of the healing of wounds, said that the substances used by surgeons were with the intention of *making* a wound heal, the tendency of the wound itself towards healing was entirely ignored. A forerunner of Sir Frank Colyer in comparative pathology, Paracelsus, speaking of the healing of wounds in the lower animals, said it is essential not to interfere with Nature.

Traumatic exposure may be likened to an incised wound, with this difference, that whereas an incised wound is intentional and the first step in a surgical operation, traumatic exposure is unintentional and to be avoided wherever possible. It was in this way that the older operators regarded traumatic exposure and they treated it as such, the first step being to arrest hæmorrhage; for this the actual cautery was preferred.

Leonard Koecker, writing in 1826 of an experience of twenty-five years, describes this operation. A candle with a very thick wick was lighted and held by the patient on a level with the mouth about 8 in. distant from it. A suitable wire bent at the requisite angle and heated to a red heat in the flame of the candle was applied swiftly and lightly to the bleeding spot. Koecker says the operator must be swift and adroit. He has in mind not merely the arrest of hæmorrhage but the creation of a scab, for, as Lister realized about forty years later, good healing takes place under a scab.

Thomas Bell denied that the actual cautery could be effectual in this way since the requisite heat could not be maintained between the candle and the bleeding spot. Perhaps Bell was not so swift nor so adroit as Koecker.

Chapin Harris, one of the pioneers of dental education and dental journalism in America, writing in 1839 and speaking also of twenty-five years' experience, gave a valuable summary of all the various methods of treatment of the exposed pulp. He says: "The fact that the vitality of the tooth can, in many cases, be preserved after the lining membrane has been exposed being admitted, question arises, does pulp remain in the same condition as it is at the time of operation?" (It is interesting to remember that the same question was asked last year in the discussion on Mr. Stewart Ross's paper.) Harris continues: "When the treatment of teeth in which the pulp has been exposed by caries, is better understood, a greater proportion of vital teeth will be preserved. A healthy living tooth is less likely to become obnoxious to the surrounding tissues than one which has been deprived of a large portion of its vitality."

He next discussed the capping of pulps, or, as it was expressed at that time putting little helmets over the exposure with the idea that there was a vacuum between the

the infected area and along the sinuses without conspicuous success, though one patient had a period of five and a half months freedom from symptoms before recurrence, after a history of a sinus breaking down every fortnight. Seven patients, including one of the sulfa drug failures, have been treated with local penicillin applied to the depths of the infected tissues by means of thin rubber tubes inserted through incisions in the skin.

In four of these patients the results were strikingly successful. Figs. 1, 2, 3, 4 illustrate two patients who received this treatment. In neither of these patients has there been any sign of recurrence after periods of nine months in the first patient and over a year in the second. In one patient the disease recurred after one course of penicillin but after a second course has not recurred in four months and in two patients



FIG. 1.

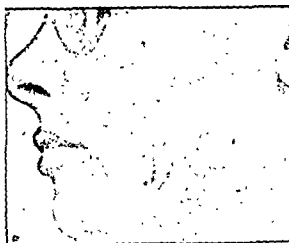


FIG. 2.

FIG. 1.—Patient had $\overline{6}$ root removed. Ten days later soreness and swelling developed. Swelling persisted even after intra-oral incisions. Condition shown is two months after removal of root.

FIG. 2.—Same patient seven months after penicillin treatment, before scar removal.

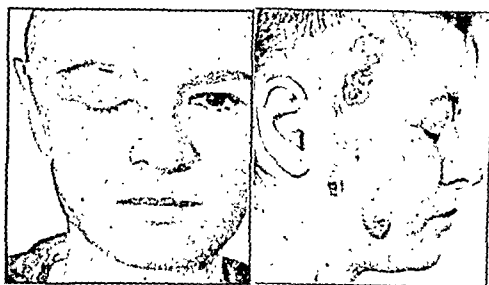


FIG. 3.—Patient had $\overline{8}$ removed, swelling and trismus started soon after. Photographs show condition five months after the extraction.



FIG. 4.—Same patient fifteen months after completion of penicillin treatment, before scar removal.

penicillin failed to have any effect on the disease at all. These results were in general agreement with the *in vitro* penicillin-sensitivity of the organisms, since the strain of organisms present in the two failures were found to be eight times less sensitive than the Oxford H staphylococcus, whereas in the successful cases the strain was of equal sensitivity or only half the sensitivity of the control staphylococcus.

This difference in sensitivity of the various strains found, makes a sensitivity test *in vitro* essential before any prognosis for penicillin treatment can be given. It also provides a further link in the chain of evidence already partly made up from observations of slight differences in morphology and cultural characteristics, suggesting that the term actinomycosis covers many strains of the organism causing varying clinical manifestations and calling for different forms of treatment.

It would appear that the time has now come for subdivision of the actinomycetes.

I would like to express my gratitude to Professor L. P. Garrod, who carried out the bacteriological work on the cases described, and also to my colleagues Mr. Rainsford Mowlem and Mr. Fickling of the Plastic and Jaw Centre, Hill End E.M.S. Hospital, for referring cases to me and allowing me to quote mutual cases.

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The next slide showed the tusk of an elephant which had been severely damaged at an early stage of development. It compared with a similar one in the human incisor which was the subject of a communication of the Odontological Society in 1886. It was sent to Mr. Storer Bennet who sectioned it.

The conditions were very much the same as that of the elephant; it is a lower incisor of a child of 13 who damaged it by a fall; the tooth was folded on itself and there had been a considerable amount of secondary dentine formed and the cement had grown under the enamel in the lower part of the fracture.

The other case was a longitudinal fracture of an upper canine also the result of a fall which drove the tooth up into the socket. The fragment was separated from the main tooth and whether the fracture calcified in the form of a blood clot or a secondary formation of secondary dentine is not certain.

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In the first section there was a mass of laminated tissue, the direction of the fracture was seen in the step-like shape on the left side where a large piece on the side of the pulp cavity had gone, whilst on the right the fracture had run in more regular and more oblique directions.

This pulp did not die or inflame but calcified—Sir Charles suggested that in traumatic exposure the blood should not be wiped away but allowed to coagulate and afterwards covered with some organic substance such as sterilized fibrin or gelatine. No inorganic materials nor strong medicaments should be applied. Hopewell-Smith's opinion was that this injury had three years in which to recover and complete the development of secondary dentine not by conversion of the blood clot nor organization of inflammatory products but simply by conversion or secretion of lime-bearing cells of the pulp into one united mass.

Mr. Kenneth Hooper: Mrs. Lindsay has pointed out that in the animal kingdom and in human teeth the dental pulp does show remarkable recuperative powers. She drew attention to Mr. E. B. Manley's invaluable work on filling materials, in which he has demonstrated a matter of great importance, viz. the very innocuous nature of zinc oxide and eugenol on the dental pulp, emphasizing to the profession how much more widely this excellent mixture should be employed. Some years ago Mr. Fry told me that he covered exposed pulps with small discs of blotting paper and I have followed this method. The blotting paper is moistened with eugenol and is placed over the minute exposure and the cavity is filled with a mixture of zinc oxide and oil of cloves. It is very rarely that any discomfort is experienced when the effect of the local anæsthetic I have used wears off.

Mrs. Lindsay asked: Is the pulp killed by kindness? It has always been realized that the pulp at the point of exposure was infected and excessively caustic disinfectants have been used with disastrous results.

Quite fantastic claims have been made in America in extolling the use of the sulphona-mide group of drugs for this purpose and I suggest they should be tried more widely over here. It appears to me that penicillin should be better still, since it is so innocuous to the most delicate tissues. I have started to use penicillin cream, of the strength of 500 Oxford units to the gramme.

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helmet and the pulp. Harris very wisely says it is impossible to have such a vacuum for an exudation from the pulp will fill the space and subsequently calcify. He recognized such a condition when the teeth are excessively worn down by attrition: "A beautiful provision of Nature to protect these delicate and highly sensitive organs." He calls this tissue callus or more properly speaking osteodentine.

Hullihen, the inventor of the screw forceps for the extraction of roots, copied this work of Nature in his operation for the preservation of the vitality of the tooth. He first filled the tooth, then with a spearhead drill, a line above the alveolar crest, drilled into the pulp chamber inducing a flow of lymph which he hoped would calcify. As Harris says: "From the very frequent failures of this operation it is not now performed."

Another method was to mummify or tan the pulp by the application of the soft centre of Aleppo oak galls. Harris says it must be admitted that this treatment failed more often than it succeeded.

As the years passed it became evident that these attempts to preserve the vitality of the teeth were not successful and in 1886 L. Jack writing in the "American System of Dental Surgery" says that the pulp died by asthenic metamorphosis without giving evidence of a single pang: "This gives the operator a sense of false security."

For the next few years the orthodox teaching was devitalization of the pulp, and ingenuity was taxed to produce various methods of filling root canals, each method claiming perfection. However, at the beginning of the new century this complacency was dispelled by two ominous things. (1) Focal infection, and (2) the publication by Hess of Zurich, of his method of demonstrating the anatomy of the root canals.

The idea of the former was seized by the medical profession as the solution of many of their cases of difficult diagnosis and wholesale extractions followed. Later there began to be heard one or two voices raised against this orgy of extraction when articles headed "Should all Pulpless Teeth be Extracted" and "The Problem of the Pulpless Tooth" began to appear.

Hopewell-Smith said that the human pulp is endowed with a nervous delicacy of function and perception wholly unnecessary for mere nutritional purposes. The sensory nerves are concerned with translating the various forms of stimulation into the perception of pain. This is a sign that during the course of evolution there has been developed and established a defence mechanism of an unusual kind to meet the singular requirements of the modern human dentition. He agreed with others that the pulp resents interference and will endeavour to protect itself without any clinical signs. The preparation of a living tooth for a crown is an affront to Nature, the tissues are permanently injured. When purulence arises it is due to the rigid quality of the walls and the fact that there is no collateral circulation to remove the products of inflammation. He agreed that it is possible for an injured pulp to heal and gave the description of the case sectioned by Sir Charles Tomes.

Clyde Davies said that the pulp was above the average of the other connective tissues of the body in its ability to resist surgical interference; he advocated that after exposure the pulp should be amputated, and gives several cases in which after such an operation the rest of the pulp tissues calcify.

Sir Frank Colyer's slides of the elephant tusk showed how a tooth of persistent growth could recover after gross injury. [Slides were then projected.]

The first slide showed the condition of the tusk which has been sectioned in four places. The first section showed a condition of coarse tissue with an intermittent surrounding of cement. The second one showed a more regular condition of secondary dentine with the cement surrounding broken by the rough tissue. In the next section the cement had nearly closed and showed a little break with overlapping. In the centre of the almost perfect ivory were one or two seeds, and, lastly, there was an evidence of complete recovery showing the normal ivory of commerce.

The elephant tusk being of persistent growth might seem to have advantage over teeth of limited growth but one slide showed the partially developed incisor of a Malay bear which had been damaged at an early stage of development. A furrow running longitudinally through it in transverse section appears to be folding the tissues into one another.

When there is sepsis there is an endeavour to wall it off. Mr. Stewart Ross showed this condition and in a recent article in the *British Dental Journal* by Professor Herbert, the same condition is shown in the human pulp.

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Professor W. E. Herbert: The recuperative powers of the various tissues depend in the main on the richness of their blood supply and the severity of the injury or infection. The dental pulp is no exception, and clinical evidence shows that in a developing tooth recuperative powers are good. They become less good when the root is fully developed and the blood supply is reduced to one or two vessels passing through small apical foramina, and still less good in older patients when the blood supply is further reduced by additional deposits of cementum.

Anything which increases the blood supply increases its recuperative powers. A method of doing this was advocated in an article written in Czechoslovakia before the war which suggested boring a hole with a sterile bur through the gum, outer plate of bone, cementum and dentine so as to establish a collateral circulation between the pulpal and gingival vessels. This would seem to be a rather rash procedure to carry out upon a tooth already injured and hardly to be contemplated as a prophylactic measure against future injury.

A similar result is, however, often obtained in the case of fracture of the root of a tooth, and such teeth often do better than those where the crown alone is fractured.

[Radiographs were then shown of various teeth which had sustained injury, illustrating the favourable result which was often obtained in fracture of the root as a result of the establishment of a collateral circulation through the line of fracture (*Brit. Dent. J.*, 1942, 71, 62) and sometimes in other cases as a result of calcification of the entire pulp chamber (*Brit. Dent. J.*, 1941, 70, 369).]

It is true that when infection reaches the pulp from a carious cavity there is an endeavour on the part of the pulp to wall it off. This endeavour is, however, usually unsuccessful, extension of the pulpitis occurring later even though the pulp remains comfortable and vital for a time.

Clinical results from capping an exposed pulp are on the whole disappointing. The most hopeful course in carious cavities would seem to be to avoid exposure in those cases when the pulp is thought to have a chance of recovery, leaving a sedative dressing for a time whilst further deposits of secondary dentine are laid down.

Mr. K. Strauss: What interested me especially were the slides Mrs. Lindsay showed demonstrating the results of Mr. Manley's experiments with the implantation of dentine dust in the dental pulp.

My attention was directed first to similar investigations, carried out by Professor Neuwirt of Prague and published in "*Zubní lékařství*" (1928) and in the *Zeitschrift fuer Stomatologie* (1933), amplified by personal communications. Mr. Manley's slides appear to confirm Prof. Neuwirt's findings most satisfactorily. Numerous papers by Feldman (Moscow, 1932), Hellner (Stockholm, 1930, 1933) et al., arrived at similar conclusions.

For practical purposes, the choice rests between one of the following preparations: (1) Autogenous dentine dust, i.e. dentine dust obtained from the tooth to be treated itself; (2) heterogenous dentine dust, i.e. dentine dust which has been prepared in advance and stored for future use; (3) a commercial calcium hydroxide preparation "Calxyl". Dentine dust appears to be giving the best results. I prepare and use heterogenous dentine dust for my own cases. It is important that no other drug, except for a 3% hydrogen peroxide solution must be employed. Neither escharotics, such as phenol or creosote derivatives, nor alcohol or other irritating or dehydrating drugs must be brought into contact with the pulpal tissues.

I have employed in my own practice this so-called "biological" pulp treatment exclusively for the last eight years, in the case of exposures as well as of root treatment, with the most gratifying results.

Mr. Stewart Ross said that the whole problem of root canal therapy as practised on the exposed vital pulp, rested on the one salient fact that bacteria were always present in the pulp chamber of every tooth with an exposed carious cavity. Owing to the surrounding dead dentine and patent tubules, it was almost an impossibility to destroy all the organisms without destroying the pulp. Strong antiseptics injured the delicate connective tissue of the pulp, thereby presenting the remaining organisms which inevitably survived with a fruitful field in which to grow and multiply. The only sure way to destroy the bacteria was to kill the pulp, having first cauterized the cavity and burnt out the pulp tissue by means of the electric hot point. Mr. Stewart Ross drew attention to Sir Frank Colyer's pictures shown by Mrs. Lindsay of an elephant's tusk, which had sustained an injury, and new dentine was shown to have been laid down towards the growing end of the tooth. He pointed out that this was not a reaction to the injury, but simply the normal laying down of dentine by odontoblasts in a tooth of persistent growth.

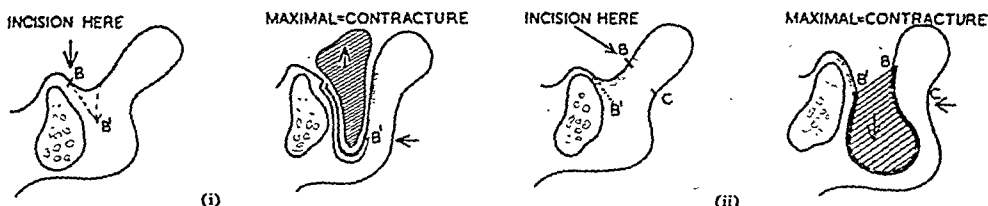
[May 28, 1945]

Epithelial Inlays to the Labial Sulcus of the Mandible

By E. A. HARDY, L.R.C.P., M.R.C.S., L.D.S.E.

IN a Casual Communication on a method he advocated for skin-grafting the labial sulcus of the mandible Fickling (*Proc. R. Soc. Med.*, 1945, 38, 199) suggested that the incision should be made, not at the junction where the mucous membrane met the mucoperiosteum of the alveolus, but where the lining membrane joined the body of the lip, "in order that the 'contraction line' may develop at the correct level". I fully agree with him that this line tends to be the site of great contraction, but differ from him in it being the site of election, because in my experience there are disadvantages in this position.

The first disadvantage, though small, is of some importance. The membrane lining the sulcus is very loosely attached and when divided at the point he advocated, it does not become any more adherent to the alveolus in its new position. We all know what it means to fit dentures where the soft tissues are freely movable over the alveolus.



Mr. Fickling's fig. 2, modified to illustrate Mr. Hardy's text. Less severe loss of buccal sulcus. (i) The normal point of incision makes the mucous membrane-graft junction too low. (ii) Incision made toward the free margin of the lips so that the mucous membrane-graft junction occurs at a level giving the best facial contour.

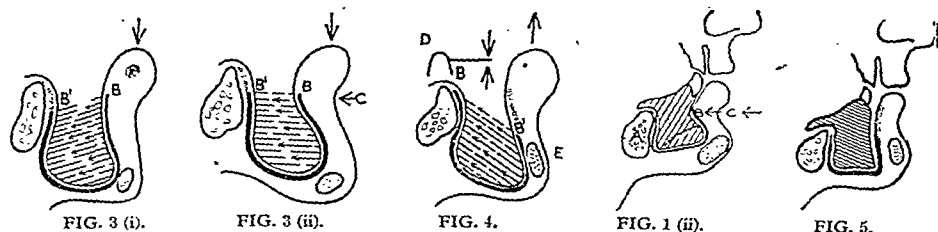


FIG. 3.—Diagrams show by means of arrows the lines of force acting on the mould and affecting the lip at the beginning (i) and the end (ii) of the first three weeks after operation when the swing of the mucous membrane is as fig. 2 (ii). FIG. 4.—Arrows show the lines of force acting on the mould, lip and splint when the mucous membrane is swung, as advocated by Mr. Hardy and shown in fig. 2 (i). D. Splint. E. Pad of fat.

FIG. 1 (ii) from Mr. Fickling's series.

FIG. 5.—Shows an alternative position of the pad of fat in relation to the prosthesis.

Secondly, although it is commonly recognized that the whole graft contracts, my experience has taught me that this contraction takes place *mostly* over muscle and fibrous or scar tissue, less over subcutaneous tissue and least over bone. It follows, then, that the more of the graft in contact with the bone and the less in contact with soft tissues, especially the muscle and pad of fat of the chin, the easier will be our task when we try to control shrinkage.

Thirdly, Fickling's contraction line tends to depress the lip line and the point of the chin whilst Gillies' line tends to elevate it. This drooping chin necessitates restoration. Therefore, in the final appliance Fickling restores the contour by cutting away the central position of the mould. In my twenty years' experience with Sir Harold Gillies up to the beginning of this war I have never found this necessary.

Let me explain this still further by elaborating Mr. Fickling's diagrams.

It will be seen on referring to his illustrations that he did not advocate the incision and swing of the mucous membrane from the point B to B' in fig. 2 (i) but from B to B' in fig. 2 (ii).

To make it clearer I have shaded in the swing of the mucous membrane in each case. I agree with him fully that the contraction tends towards an upward thrust of the mould in (i) and downwards in (ii) and also agree that there is a marked contraction at his "contraction line" BB'. Figs. 3 (i) and (ii) demonstrate by arrows the lines of force (caused by the contraction of the graft) acting in the mould and affecting the lip and chin. It will be readily seen how in those early days of the graft there is a greater tendency to contraction and a serious depression of the lip-line. It will also be observed that if B is allowed to contract towards B' too soon so, as to increase groove C, the difficulties of removing the bulk of the mould are greater. I suggest that it was because of this that Mr. Fickling had to reduce the central portion of the mould and the improvement in profile was due to a return of the lip-line to its proper level.

The advantages of the other method are demonstrated in fig. 4. Here it will be seen that the lines of force tend to extrude the mould. But as the splint prevents this the graft is kept on the stretch during that all-important period, namely, the first three weeks. That indefinite period, depending on so many factors which we know so well, when contraction ceases, has in my experience become more determinable.

The position of the pad in relation to the grafted pocket. All prosthetic appliances are made to replace loss of hard, bony tissue. When the thumb is placed on the point of the normal chin, bone is felt and not the pad of fat; this is in front and above. The pad of fat, therefore, should be in the same relation to the prosthesis as it represents the symphysis menti (fig. 5) and not be in the position shown in Mr. Fickling's fig. 1 (ii).

Visual Education in Dentistry. [Abstract]

By Flight Lieutenant H. MANDIWALL, M.B., B.S., L.D.S., F.R.P.S., R.A.F.

THE often quoted Chinese proverb "A picture is worth ten thousand words", is getting out of fashion now, for a really good picture is worth "X" times more than what the proverb suggests, the value of "X" depending upon the quality of the picture and its ultimate use. Visual education should be of paramount importance, as the educationists tell us that about 90% of what we learn passes through the eyes, and also that what we see is believed to be more authentic and impressive than what we hear.

A technical discussion of almost any subject before an average group is understood only by those who have had training in that field. The same discussion presented in the usual language, might become clear and understandable to most of us, if a few pertinent illustrative materials were used.

In the future the method, rather than the amount, of teaching will matter most. The days are fast dwindling when the professor came and lectured to the students by reading *ad verbatim* lines from his favourite book. The lecturer nowadays usually dispenses with his notes and gives as it were a running commentary with the visual aids which impress the mind forcefully and permanently. If we just cast back our eyes to our books we must confess that illustrations and drawings conveyed to us much more than hundreds of words. Dental knowledge can be imparted in three ways, by the lecturer, by books, and by visual aids. Photography will never entirely replace the lecturer or books but it will materially help both of them to an extent which has never been dreamt of in the past.

The extent to which these valuable aids are used, and the degree of effectiveness with which they will be employed in any teaching situation, will depend almost entirely upon the amount and the quality of the training the teacher has received. The greatest factor retarding the more extensive and the more intelligent use of visual aids is the inadequate training of teachers to make use of the materials available.

In the modern school: (a) Visual material will not supplant the textbook or teacher

but will supplement and increase the effectiveness of the teacher and text. Hence the term "Visual Aids"; (b) visual aids are most effective when closely correlated with the curriculum; (c) the most effective visual lesson is one that is treated as any good lesson should be; teachers must prepare for the visual lesson in advance. They should be familiar with visual aids before presenting them; (d) the visual materials must be available at the precise moment when wanted by the teacher; (e) visual aids should be excellent in quality and accurate in detail. Misinformation obtained through visual aid is inexcusable; (f) a few appropriate illustrations are better than a score of less related ones; (g) visual aids should make accessible in the classroom that which is otherwise inaccessible; (h) no one type or class of visual aid should be used to the exclusion of others. Each has its own use and value.

While concrete materials are essential in the development of various types of learning, the ends of instruction are generalization, understanding, integration, &c.

Verbalism may be defined as the generic term applied to the use of words without appreciation of the meaningful content of the words, or of the meaningful content of the context in which they are used. It is to eliminate this verbalism that this paper is written. Verbalism may assume any one of many forms. For instance if our sense or meaning is known, but if the words are used in another and different sense, the outcome is verbalism. In part, verbalism is the result of instruction on an abstract level—a level which makes no provision for the depth and variety of concrete experience necessary to give richness to the abstraction. The ancient maxim—the concrete precedes the abstract—has been so readily accepted as obvious, that its full significance and application to learning have been universally overlooked. That old dictum can be re-worded in the light of modern teaching and experience as follows—if the abstraction is to possess a richness of meaningful content, the concrete must precede the abstract in breadth, depth and variety towards progressive stages of abstraction.

In mass instruction visual aids must be used to enrich and vary the pupil's concrete experience.

Whilst motion pictures and lantern slides are valuable visual aids, they are by no means the only aids available to the instructor, neither are they the ones most widely used in education. A visual aid is any picture, model, object or device which provides concrete visual experience to the student for the purpose of (1) introducing, building up, enriching or clarifying abstract concept, (2) developing desirable attitudes, and (3) stimulating further activity on the part of the learner.

There are a number of visual aids that one can utilize in education. In certain situations some will be found to be better than others. A combination of types are frequently desirable.

For convenience, these various visual aids have been classified as (a) clinical materials, (b) museum material, (c) motion pictures, (d) still pictures, (e) graphic materials. The idea behind this classification is to show progression from the most concrete to the least concrete of the visual aids.

A *motion picture* is, of course, not a picture of motion at all. Psychologists tell us that an image on the retina of the eye remains there approximately $1/12$ th of a second after the object itself may disappear from view. This is known as "persistence of vision". If we can arrange, therefore, to remove one picture and substitute another similar picture within this period of "persistence of vision", we can see the picture with a feeling of continuity just as we do the motion picture to-day. As the speed of projection of movie films ranges between 16 frames per second for silent and 24 frames per second for sound film, a smooth continuity of a series of still pictures placed close together is maintained throughout the length of the film without any break between the subsequent pictures.

Advantages of silent motion pictures.—By means of slow motion, the student is given an analysis of movement, thus enabling him to study the action which would be much too rapid for the unaided eye to analyse. To speed up action where necessary, by use of animated drawings, motion pictures can bring before any group clear representation of action which would be invisible to the unaided eye. With the aid of a microscope, the motion picture camera can be used to record and reproduce the normal or abnormal action of processes, much too small to be seen by the naked eye. The ciné film may be used to present animated diagrams or statistical data in a way that will make an indelible impression upon the audience. It may be used to provide a brief survey of

It will be seen on referring to his illustrations that he did not advocate the incision and swing of the mucous membrane from the point B to B' in fig. 2 (i) but from B to B' in fig. 2 (ii).

To make it clearer I have shaded in the swing of the mucous membrane in each case. I agree with him fully that the contraction tends towards an upward thrust of the mould in (i) and downwards in (ii) and also agree that there is a marked contraction at his "contraction line" BB'. Figs. 3 (i) and (ii) demonstrate by arrows the lines of force (caused by the contraction of the graft) acting in the mould and affecting the lip and chin. It will be readily seen how in those early days of the graft there is a greater tendency to contraction and a serious depression of the lip-line. It will also be observed that if B is allowed to contract towards B' too soon so as to increase groove C, the difficulties of removing the bulk of the mould are greater. I suggest that it was because of this that Mr. Fickling had to reduce the central portion of the mould and the improvement in profile was due to a return of the lip-line to its proper level.

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Section of Urology

President—F. MCG. LOUGHNANE, F.R.C.S.

[March 22, 1945]

Case of Pseudo-Hermaphroditism and Adrenalism.—JOHN EVERIDGE, O.B.E., F.R.C.S.

Present age 19 years, 10 months, the youngest of four. Twins prevalent in mother's family. At birth sex was undetermined. At the age of 3 Mr. Arthur Edmunds operated for hypospadias. The child was born with two teeth; walked and talked when 9 months old. At 3 years axillary and pubic hair were present. Has shaved since 9 years old. The voice broke at 12 years of age. At age 10 there was periodic abdominal pain, and at age 14 monthly discharge of blood from the urethra accompanied by headaches and more abdominal pain. From age 11 onwards has had periodical swellings of the breasts, thought to be mastitis.

Mentally bright, won a scholarship and matriculated at the age of 16. Preferred masculine pursuits and was a good athlete.

At age 14 there was an attack of acute retention of urine, requiring catheterization.

In November 1943 more severe abdominal pains suggested to his mother that the testicles (hitherto never identified) might be responsible. Pregnyl injections were used as an aid to confirmation of her supposition. These seemed to increase the pains and justified abdominal exploration for localization of the testes. At that time the 17 ketosteroids in the urine were found to be 75.7 mg. in twenty-four hours.

My laparotomy revealed female genital organs and I removed the uterus, broad ligament and left ovary. Palpation of the adrenals showed no enlargement but there seemed to be some anchoring of the upper pole of the right kidney, possibly due to some change in the right suprarenal gland.

On the 9th post-operative day there was severe bleeding from the urethra and distension of the bladder. A surgeon colleague drained the bladder and found it contained clear urine. The bleeding was therefore from the vagina. Subsequently, endoscopic visualization revealed the opening of the vagina into the urethra $\frac{3}{4}$ in. below the bladder neck. A ureteric catheter was passed into the vagina and 5% sodium iodide solution introduced. Radiography revealed a large pyriform shadow reaching almost to the dome of the bladder which was, simultaneously, demonstrated by aero-cystography (fig. 1).



FIG. 1.—Superimposed vaginogram and aero-cystogram. 5% sodium iodide solution was introduced endoscopically by ureteric catheter into the minute opening where the vagina communicated with the posterior urethra. Simultaneously air was introduced into the bladder through a metal catheter which is seen in situ.

This case is shown to promote discussion as to whether vaginectomy should be performed and what technique should be adopted. There would appear to be no indication for surgical interference with the adrenals, or of the removal of the remaining ovary, since an endocrine balance appears to have been established in this case. There has never been evidence of any sexual psychological problem.

broad topics. With the various tricks of motion picture photography, it can be used to clarify impression covering almost any situation when motion is necessary to convey the message speedily and correctly. By means of the motion picture of animated diagrams one can visualize the invisible.

But the motion picture is, at best, but a substitute for the actual experience. The projection of motion pictures requires a more thorough darkening of the room than would be necessary for glass slides. Their cost is a serious item and they are perishable. Films must be shown two or three times if any real study and analysis of the content is to be achieved. Films are used too often as a substitute for, rather than a supplement to, other methods of presentation.

Evaluation of the motion picture film.—Use motion pictures only where motion is necessary and films should not be used unless they make a definite contribution to the teaching of the subject.

Values of motion picture in instruction.—Helps initial learning of concrete factual material. Develops thought and reasoning. Helps learning relationships. Makes learning permanent. Helps to form habits and skills. Develops descriptive and explanatory responses, imagination and interest.

Visual textbooks.—The reading and study of any printed page is a “visual” *modus operandi*. Beyond the enrichment of a text through good layout and design is the possibility of that kind of text which tells its story chiefly or in great part by the use of photographs, illustrations, graphic means and other devices. No amount of good visual material will improve the poor text in a book.

Dental teaching films are only beginning to demonstrate their value. Colour and sound have vastly increased their effectiveness and the animated diagram is another fairly new technique which is being employed to excellent advantage. Films prepared for the lay public would be of a distinctly different character from those prepared for the use of the dental profession. Above all the production of a dental teaching film should be placed in the hands of a photographer with competent medical and dental background and a knowledge of what can be translated into film language without the introduction of unnecessary or unsuitable material.

Visual education is not merely a matter of persuading teachers to use mechanical contrivances in the classroom. Behind the teachers’ work is a whole set of organizational problems. The selective principle in all picture-making is the underlying logic of visual symbolism. At the root of the whole problem of visual supply are the twin processes of analysis and creation. Visual materials cannot be manufactured to order. They depend on a contribution of educational, artistic, and technical genius.

I am grateful to the Director of Dental Services, Air Commodore G. Ballantyne, D.F.C., for his permission to use the slides and films shown at this meeting.

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The following cases and specimens were also shown:

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 Gunshot Wound of Prostate and Ejaculatory Ducts. Vesiculograms.—Mr. HUGH DONOVAN.

[April 26, 1945]

Penicillin in Urinary Infections

By ROBERT CRUICKSHANK, M.D., M.R.C.P.

L.C.C. Group Laboratory, Hampstead, London

THE advantages of penicillin in the treatment of infection are its great activity against most Gram-positive bacteria and the Gram-negative diplococci, an activity which is unimpaired by the presence of blood or pus or massive infection, and its almost complete lack of local or systemic toxicity. Its disadvantages are its instability in weak solutions due to oxidizability rather than heat-lability, its inactivation by acids and alkalis (it is not affected by a range of pH from 5.0 to 8.0), and its rapid excretion so that continuous, or frequent intermittent, administration parenterally is necessary. For the best clinical use of the drug, it is advisable first to find if the infecting organism is penicillin-sensitive (this is particularly advised in staphylococcal infections for 10 to 20% of *Staph. aureus* strains are resistant), and, when treatment has been instituted, to test penicillin-levels in blood and urine. (The appropriate laboratory methods were described.) Excretion may be considerably delayed if there is kidney disease. Patients on penicillin-therapy may show some febrile reaction and the temperature chart may not be a reliable guide to the patient's response. Occasionally patients develop allergic reactions, e.g. skin-rashes, to penicillin or contained impurities.

Urinary infections may be divided into two groups in regard to the indications for penicillin-therapy. In the first group are staphylococcal infections, occurring either as a parenchymatous infection of the kidney secondary to some focus elsewhere in the body, or as a staphylococcal cystitis. Staphylococcal renal abscesses going on to renal carbuncle or perinephric abscess have not been common in the inter-war period but this type of infection was prevalent at the end of the 1914-18 war, probably as a complication of wound osteomyelitis, &c., and it may again become more common. Diagnosis is assisted by finding *Staph. aureus* in the urine and by the presence of leucocytosis. For such a condition, penicillin-therapy (say, four daily injections of 20,000 units at four-hourly intervals) should be instituted as early as possible. Staphylococcal cystitis is often a low-grade infection due to *Staph. albus*, but it is very resistant to other therapies and may respond to either systemic or local penicillin. Treatment of staphylococcal infections with penicillin should be continued for some days after clinical and bacteriological cure on account of the tendency to relapse.

The organisms responsible for the great bulk of urinary infections—the coliform group, *proteus*, *pyocyanus* and *Str. faecalis*—are classified among the penicillin-resistant bacteria. But it should be remembered that penicillin is greatly concentrated in the urine so that on a daily dosage of 60,000 to 100,000 units and allowing for a 50% urinary excretion of penicillin, concentrations of 20 to 40 units per c.c. are to be expected. Helmholz and Sung [1] have lately shown that *Str. faecalis* is inhibited *in vitro* by a concentration of 3 units of penicillin per c.c. of urine at pH 7.6, *B. proteus* by 8 units, and certain coliform bacilli by 15 to 30 units: *B. aerogenes* and *pyocyanus* resisted concentrations over 60 units per c.c. Thus penicillin might prove beneficial in urinary infections due to *Str. faecalis*, urethritis might also respond to penicillin. From experience in the treatment of gonorrhoea, systemic rather than local penicillin-therapy is indicated in these infections.

REFERENCE

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Sulphonamides in Urinary Disease

By J. C. AINSWORTH-DAVIS, Wing Commander, R.A.F.V.R.

THE introduction of sulphonamides has proved to be the greatest advance yet made in urinary disinfection, and, of the many varieties, I have found that sulphathiazole is perhaps the most useful. Sulphathiazole has a number of synonyms which include M & B 760, Ciba 3714, Cibazol, Thiazamide, B.P. 2090, Eleudron, and Neostrepsan.

Indications.—Sulphathiazole can be used both for acute and chronic infections of the urinary and genital tracts, and acts most powerfully on organisms of the coli type, streptococci (other than *faecalis*) and gonococci. It acts less powerfully on staphylococci, *B. proteus*, and *pyocyanus*, and not at all on *Str. faecalis*.

Basic principles.—(1) It is of great importance for the initial dose, or, better still, the initial two doses to be large in order to obtain the maximum concentration of the drug in the blood-stream in the smallest possible space of time, and, if the infection is very acute, it is wise to give the first dose intravenously.

(2) Sulphathiazole should be administered four-hourly for at least two days and, unless there are strong reasons to the contrary, the patient should be wakened up at night for this purpose.

(3) A white blood-count should be done before beginning the course and repeated on alternate days in order to guard against agranulocytosis. If there is a rapid fall to under 4,000 the drug should be discontinued and a differential blood-count performed.

(4) The fluid intake during treatment should be increased to at least five pints in the twenty-four hours in order that the urinary output is maintained at 3 to 4 pints at least and, to ensure this, all urine should be passed into a urinal and measured and charted. Should the output fall below 2 pints, with pain in the loin and hæmaturia it suggests blocking of the renal pelvis or ureter and calls for an immediate cessation of treatment.

(5) Sulphathiazole is more soluble in alkaline than in acid urine and, therefore, it is essential to prescribe alkalis by mouth at least three times a day in order to diminish the likelihood of crystallization in the upper urinary tract. Incidentally the drug is more fully ionized in an alkaline urine and, consequently, more effective.

(6) It is no longer necessary to withhold sulphur-containing foods such as eggs.

Administration.—For oral administration, sulphathiazole is prepared in $\frac{1}{2}$ gramme tablets which are best crushed and added to an alkaline mixture containing 20 grains each of sodium bicarbonate and sodium citrate in $\frac{1}{2}$ oz. of peppermint water and flavoured with 10 mm. of spirits of chloroform.

For intravenous use, the sodium salt of sulphathiazole is used, which is supplied as a dry powder in ampoules containing the equivalent of 1 gramme. The contents of an ampoule are dissolved in 10 c.c. of sterile distilled water immediately before use. Every patient undergoing sulphathiazole therapy should be provided with a chart on which the doses are clearly marked together with the times that they should be given. This chart represents a full course of sulphathiazole for a moderately severe infection in an adult. With the exception of the first two doses, which consist of two grammes each with a four-hour interval, the course consists of 1 gramme, or 2 tablets, four-hourly for forty-eight hours, 1 gramme six-hourly for forty-eight hours, and finally 1 gramme eight-hourly for forty-eight hours which makes a total of 29 grammes spread over six days. The day and time are entered against the doses and there are additional columns for the fluid intake, whether by oral or some other route, and the output, which should include not only the amount of urine passed, but also any fluid lost by vomiting and bowel action. There is a column on the left hand bottom corner for the leucocyte count both before the course and on alternate days. For severe infections endangering life the doses should be increased by 50%, that is to say $1\frac{1}{2}$ grammes instead of 1 gramme and an intravenous injection of from 2 to 4 grammes as a preliminary measure.

For mild infections or for prophylaxis against "urethral" fever, which may follow decompression of the bladder by an indwelling catheter or per-urethral resection of the prostate or some other procedure, the doses should be diminished by 50%. That is to say $\frac{1}{2}$ gramme is given instead of 1 gramme. For children up to 3 years the dose is one-third, from 4 to 10 years half and from 11 to 15 years two-thirds, respectively, of the amount given to adults.

Complications and their treatment.—Apart from nausea, headache and cyanosis, which do not need any special treatment, there are three main complications which call for immediate stopping of the drug. These are primary or acquired hypersensitivity, agranulocytosis, and blocking of the renal tubules, pelvis and ureters with crystals.

Primary or acquired hypersensitivity (or drug fever) is shown by rise in temperature during treatment or within twenty-four hours of its cessation. If the course is a first one, fever rarely appears before the eighth day but may come on much earlier if previous courses have been given. It is sometimes difficult to distinguish it from the fever due to the infection, unless other physical signs point to the latter. With a true drug fever the temperature will fall abruptly when the sulphathiazole is stopped, while a rise in temperature some days after the end of the course indicates a lighting up of the infection and calls for another course of treatment.

†Agranulocytosis.—A mild degree of leucopenia, alone, need cause no alarm, but with a rapid fall to below 4,000 per c.mm. the drug must be stopped and a differential leucocyte count made. If the white count falls to below 2,500 per c.mm. the condition should be

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Sulphonamides in Urinary Disease

By J. C. AINSWORTH-DAVIS, Wing Commander, R.A.F.V.R.

THE introduction of sulphonamides has proved to be the greatest advance yet made in urinary disinfection, and, of the many varieties, I have found that sulphathiazole is perhaps the most useful. Sulphathiazole has a number of synonyms which include M & B 760, Ciba 3714, Cibazol, Thiazamide, B.P. 2090, Eleudron, and Neostrepsan.

JOINT DISCUSSION No. 2

Section of Urology with Section of Obstetrics
and Gynæcology

Chairman—F. McG. LOUGHNASL, F.R.C.S.

(President of the Section of Urology)

[May 24, 1945]

DISCUSSION ON URINARY COMPLICATIONS OF PREGNANCY

Mr. J. Gabe [Abridged]: As early as the third month of normal pregnancy changes take place in the upper urinary tract, gradually becoming progressive and most marked in the later months and rapidly retrogressing in the puerperium. They occur more frequently and are generally more pronounced in the right kidney and ureter than in the left. Part of this difference is accounted for by the anatomical relations of the right ureter, which, crossing the common iliac vessels almost at right-angles, lies in a position more exposed to pressure by the gravid uterus than the left, which enters the pelvis almost parallel to the vessels.

The anatomical changes most frequently seen are dilatation of the calices, the pelvis and the ureter as far down as the pelvic brim. The abdominal ureter is frequently elongated, and may become tortuous, kinked and laterally displaced. Its diameter increases, varying from 1 cm. to over 2 cm. Kinking usually affects the upper third of the ureter and may be so marked as to obstruct ureteric catheters (see fig. 1). Bands of fibrous tissue have been found between the kinks, most evident when there has been



FIG. 1.—S. D., aged 21, primipara. 30 weeks pregnant. Intravenous pyelogram at 30 minutes.

infection during pregnancy. Hofbauer described marked hypertrophic changes in the outer muscular layer of the pelvic ureter, the so-called sheath of Waldeyer, affecting the lower 3 to 6 cm. This thickening of the ureter can sometimes be detected on vaginal examination.

Even before the uterus is large enough to exert pressure, certain physiological changes occur, viz. atony, relaxation and stasis. These may precede visible pyelographic changes, and are generally regarded as being due to the action of hormones elaborated by the placenta. If the urine of pregnant women is injected into virgin rabbits, changes are produced in the urinary tract of these animals similar to those which occur in the pregnant animal. Van Wagenen and Jenkins in experiments on pregnant rhesus

regarded as an agranulocytosis, especially if the neutrophil leucocytes drop to below 1,000 per c.mm., and if there is pyrexia, lassitude, headache and sore or ulcerated throat. This complication is more likely to occur when treatment is prolonged to over fourteen days of continuous sulphathiazole therapy. Apart from stopping the drug, treatment consists of copious fluids and repeated transfusions of fresh blood.

Blocking of the renal tubules, pelvis and ureters is due to the deposition of crystals of sulphathiazole. It is one of the less soluble of the sulphonamides and crystallization is more likely to occur in the presence of partial obstruction in the urinary tract or if the patient is vomiting or sweating. To prevent this complication the fluid intake is increased to at least 5 pints in the twenty-four hours, in order to keep the kidneys thoroughly flushed out, and alkalis are given, as sulphathiazole is more soluble in alkaline urine than in an acid one.

Urinary blockage may occur at any time during treatment, and has been known to follow small amounts of sulphathiazole such as 5 to 10 grammes by mouth or even one large preliminary intravenous injection. The finding of crystals in the urine, though an indication for caution, is not a bar to treatment providing the urinary output is satisfactory and there is no renal pain or hæmaturia.

Symptoms and signs.—(1) Pain—which may take the form of renal colic or renal aching or may be felt vaguely all over the abdomen. It is sometimes difficult to distinguish the pain of a crystalline block from the pain which may be present from a renal lesion being treated with sulphathiazole. (2) Oliguria and anuria: The urinary output may fall and, in some cases, may cease altogether. (3) Hæmaturia—which may be microscopic or macroscopic and (4) A rise in blood urea sometimes to 200 mg. % or even more.

Treatment.—Should one or more of these signs be present, the drug must be stopped immediately and the fluid intake by mouth increased to 10 pints in the twenty-four hours, providing that complete suppression has not occurred. Warmth is applied to both loins by hot-water bottles or by short-wave therapy. In early cases these measures are usually sufficient to raise the urinary output and to re-establish normal urinary function, but if there has been marked oliguria for twenty-four hours, or complete anuria for 12, especially if vomiting is occurring, four additional methods of treatment are available.

A. *Massage.*—In the absence of special apparatus, the lower ends of the ureters are massaged *per rectum* in the knee-elbow position, after which the patient is turned on to his back and the kidneys and upper ureters massaged from above downwards as suggested by Major Flynn. One-fifth normal saline with 4% glucose, as suggested by Naunton Morgan and Avery Jones, are then administered by intravenous drip. Should this not have the desired effect, further massage is carried out. Morphia may be given for pain.

B. *Ureteric catheterization.*—After anæsthetizing the urethra, preferably with 0.5% cocaine-bicarbonate solution, one or both kidneys are catheterized, though this is often difficult as gritty obstruction may be encountered in the ureters and catheterization only possible on the relatively less obstructed side which, however, suffices as a life-saving measure. The renal pelvis or pelvis are washed out with 2.5% sodium bicarbonate solution until the return flow is clear, and the catheter left in situ, after removing the cystoscope, until the urinary flow is fully re-established.

The result of this treatment is often dramatic and there is no subsequent renal damage.

C. *The ureteric corkscrew* (see *Brit. J. Surg.*, 1943, 31, 34). This consists of a spiral wire ending in a knob distally, to prevent laceration of the ureteric wall, and continuous with a long straight wire proximally which passes through a stout ureteric catheter. The distal end of the wire is welded to a mount, which tops the catheter, and its proximal end to a milled thumbscrew to facilitate rotation.

It was Hamilton Bailey who first suggested to me the use of this instrument in sulphathiazole anuria, and, accordingly, if ureteric catheterization fails on account of gross obstruction in the ureter, an operating cystoscope is passed and the ureteric corkscrew is inserted first into one ureteric orifice and then into the other. Ureteric meatotomy will not be found necessary. By a process of gentle onward pressure and clockwise rotation, the corkscrew will usually be found to pass above the obstruction and, on withdrawal, will bring with it into the bladder a mush of sulphathiazole crystals, blood and mucus. If successful on one or, better still, on both sides, intravenous one-fifth normal saline with 4% glucose is given straight away.

D. *Nephrostomy.*—If the foregoing methods fail, unilateral or bilateral nephrostomy and pelvic lavage with 2.5% sodium bicarbonate solution must be carried out as a life-saving measure and followed by intravenous fluids.

SUMMARY

Although sulphonamide therapy constitutes perhaps the greatest advance in the treatment of urinary infections it is important to try and prevent the possible urinary complications by organized administration, frequent white blood counts, increased fluid intake to at least 5 pints in the twenty-four hours, and alkalinization of the urine.

For those inexperienced in this form of therapy the Medical Research Council War Memorandum No. 10 on the medical use of sulphonamides makes useful reading.

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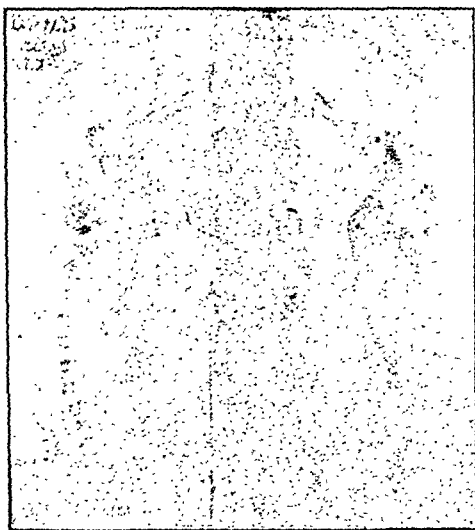


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monkeys removed the foetus by abdominal hysterotomy, without disturbing the placenta, and found that the typical pyelographic changes in pregnancy which had already occurred remained and even increased. When the placenta was removed rapid retrogression took place.

In the human subject Traut, McLane and Kuder found progressive decrease in the peristaltic activity and tone of the ureters between the 6th and 8th months with gradual recovery of tone prior to parturition. Hundley and his co-workers, by giving large doses of progestin to non-pregnant women, diminished ureteral peristalsis. The amount of prolan B and œstrin excreted in the urine of pregnant women increases as the pregnancy advances. Hundley suggests that prolan B is responsible for the atony and œstrin for the hypertrophic and vascular changes taking place in the ureter.

The stasis and atony which occur are the perfect prerequisites for infection and it is remarkable that this does not occur more often. Residual urine is found in both renal pelves. Average figures in primiparae vary from 35 to 50 c.c. for the right and are about 30 c.c. for the left. In multiparae the figures are definitely less. Stasis occurs in 73% of primiparae and 45% of multiparae and when excessive may cause temporary renal impairment; but as a rule the total renal function is unaffected, there are no changes in the blood chemistry, and renal cortical changes do not occur.

After normal pregnancy *retrogressive changes* occur in 60% of women within two weeks of delivery and intravenous pyelograms are usually normal by the 10th day of the puerperium. Ureteral atony takes longer to recover and may persist for a fortnight and even two months. Return to normal may be delayed still further and may not take place if there has been preceding pyelonephritis. Delay in retrogression may be due to scarring and infiltration of the walls of the pelvis and ureter. The normal pregnancy changes occur also in the presence of anomalous kidneys and other pathological conditions. Most pre-existing hydronephroses become larger and retrogressive changes in them are slow and often incomplete.

As pregnancy progresses the bladder becomes flattened from above downwards. In cystograms it is often saddle-shaped. Cystometric studies reveal loss of bladder tone and increased capacity, resembling closely the changes which occur in the upper tract. When atony is present renal pelvic pressure is found to be directly proportional to the bladder pressure.

Cystoscopic appearances.—In non-pregnant women the ureteral effluxes occur on an average about six times a minute. During pregnancy, especially during the time atony and stasis are most marked, effluxes are generally infrequent and the intervals between them may be prolonged from five to fifteen minutes. Feeble effluxes are commoner on the right side than the left, and are more usual in primiparae than in multiparae. There is delay in excretion of dyes and of compounds used for intravenous pyelography. Residual urine is found in 64% of parturient women and this, together with atony, is a frequent cause of retention in the puerperium, especially if labour has been prolonged. In most women bladder atony passes off by the third day.

Pyelonephritis.—Well over half the cases of pyelonephritis occur in women with various renal and other abnormalities in the urinary tract ante-dating pregnancy. When an attack clears up completely the chances of a recurrence in a subsequent pregnancy are 1 in 5, but if the urine remains infected the risk is greater, namely, 1 in 2. In persistent infections of long duration, especially with evidence of renal damage, pregnancy should be forbidden. If infections clear up completely it would be a wise policy to wait anything from six months to two years before further pregnancy is contemplated. Operations on the kidney should always be the last resort and be reserved for cases with serious complications. Corrective surgery after pyelonephritis is reserved for such conditions as ureteral stricture, which can be dilated by cystoscopic methods, and for adhesions and kinks of the upper ureter and renal pelvis. Decapsulation, nephrostomy and nephrectomy each have their indications.

Ureteral catheterization still has a place in treatment. Stasis and dilatation can be relieved by a ureteric catheter left in for two to three days. Following its use, however, several fatal cases have been recorded of uretero-arterial fistula between the ureter and the common iliac artery.

Bladder complications.—The bladder may suffer injury during labour and on cystoscopy will show œdema and ecchymoses.

Cystitis may be due to pressure of a retroverted gravid uterus, injury during labour, careless catheterization, and following pelvic cellulitis. Infection may ascend to the upper urinary tract. Treatment depends on the infecting organism. The worst cases lead to devitalization and sloughing and will end up with vesico-vaginal fistulae. Rupture of the bladder usually results from operative interference with the bladder full but may be spontaneous or may follow sloughing. Vesico-vaginal rupture follows for-

ceps or operations on the foetal head in difficult labour. *Intraperitoneal rupture* usually involves the upper posterior part of the bladder. It may be spontaneous, due to over-distension, but more commonly follows sloughing. Treatment of intraperitoneal rupture is immediate abdominal section, suture of the rent, and drainage.

Urinary calculus.—Space does not permit a detailed account of urinary calculus, occurring during pregnancy.

If a woman is known to harbour a calculus she should be advised to have it removed before embarking on any future pregnancy. The condition is distinctly uncommon. Calculus in the urinary tract is commonest in the years between 30 and 50, whereas the majority of pregnancies occur before 30.

Vesical calculus complicating pregnancy is very rare. A large calculus has been known to obstruct labour.

Suppression of urine, due to impaction of bilateral calculi or unilateral impaction with suppression on the other side, requires immediate treatment, both systemic and operative.

Tuberculosis of the urinary tract.—Tuberculosis of the urinary tract complicating pregnancy is infrequent and usually presents itself as a sterile pyuria. Although pregnancy is occasionally tolerated surprisingly well, most cases are definitely made worse by it. The symptoms exacerbate, the renal function deteriorates, and pyelographic films show increasing destruction.

Neoplasms.—Neoplasms of the urinary tract complicating pregnancy are rare. Adenocarcinomata and atypical tumours of the kidney have been described.

Solitary kidney.—The commoner causes are congenital unilateral kidney and previous nephrectomy for tuberculosis, hydronephrosis and congenital malformations. Less common causes follow nephrectomy for tumour, calculus and chronic infection. If the kidney is healthy it undergoes the usual pregnancy changes; if not, these are modified by whatever condition is present. After nephrectomy for tuberculosis, provided three years have passed and there is no evidence, after careful investigation, of involvement of the other kidney, pregnancy may be permitted. Following nephrectomy for non-tuberculous infections a woman should wait at least six months before contemplating pregnancy. In the presence of an abnormal solitary kidney, pregnancy is absolutely contra-indicated, and should it occur therapeutic abortion and even sterilization may be required. If the solitary kidney was normal before pregnancy it usually maintains its function very well, unless complications arise. These actually are no more frequent than in women with two kidneys. If pyelitis or toxæmia supervene, pregnancy should be terminated forthwith in the interests of the mother. In every case where pregnancy is allowed to continue, constant supervision is necessary.

Conclusion.—I would strongly advocate a full urological investigation in all cases with a previous history of urinary disease, and for all patients slow to recover from an attack of pyelitis or who readily relapse. If we are to prevent some of these complications, which are known to lead to chronic ill-health and even invalidism, we must obtain closer co-operation between the general practitioner, the obstetrician, and the urologist than has been the case in the past. As routine measures microscopic and bacteriological examination of the urine and an increasing use of intravenous pyelography are minimal requirements.

I desire to acknowledge my indebtedness to Miss Amy Fleming for her great help and her continued interest while writing this paper.

Miss Gladys Dodds: Pyelonephritis, or as it is more often called pyelitis, is a common complication of pregnancy. It is of interest both to the obstetrician and the urologist and one in which the workers in these two specialties must co-operate if the final effects of the disease which has started in pregnancy are to be elucidated. The early stage of the disease is seen by the obstetrician and I propose to tell you of some observations made on 287 cases of antenatal pyelitis admitted to University College Hospital during the years 1927 to 1944.

The average age of the 287 patients with antenatal pyelitis was 25.4, whereas the average age of 500 consecutive antenatal patients was 28.4. The disease is therefore one of the younger pregnant woman. This is correlated with the finding that the disease is commoner in primigravidae than in multiparæ. 185 of the patients were primigravidae and 102 multiparæ (9 of the multiparæ give a history of pyelitis in a previous pregnancy).

History of previous urinary infection.—Of the 287 patients only 38 gave a history of previous kidney disease. 18 were primigravidae, 4 of whom had had acute pyelitis shortly after their marriage. 9 of the 20 multiparæ had had pyelitis during a previous pregnancy.

Clinical course of the disease.—The onset is sudden in the majority of cases with acute stabbing pain referred to one or other side of the abdomen, often associated with

an attack of shivering, occasionally with frequency of micturition, and still less often with vomiting. The acute stage lasts a few days in the majority of patients and thereafter with treatment the patient's general condition improves, the temperature subsides, the patient feels well and is symptomatically cured. The urine may or may not still be infected.

In a small number of cases, 30 (10.4%) in this series, the disease runs a more unfavourable course, the temperature may remain high, the general condition of the patient may not improve, the quantity of pus in the urine may not diminish, anaemia may develop as a result of the prolonged sepsis, or jaundice may occur or evidence of renal failure may supervene; either diminished excretion of urine may be noted or increase in the nitrogen content of the blood may be found. Dilatation of the kidney pelvis and of the ureters may be marked, and the excretion of intravenous dyes and pyelography media delayed.

Immediate prognosis.—(a) *Mortality:* Of the 287 patients two died after the pregnancy had terminated—one the day after spontaneous premature labour at the 29th week and the other nine days after hysterotomy at the 23rd week.

Both these patients had been ill for several weeks before admission to hospital, one eleven weeks and one seven weeks. At post-mortem examination in one there was a mild degree of pyelonephritis with only slight dilatation of the kidney pelvis and no dilatation of the ureters; in the other there was a pyelonephritis with acute inflammation of the kidney pelvis and ureters. The right ureter was slightly dilated.

Death in these two cases probably occurred because of delay in receiving effective treatment.

(b) *Cure rate during pregnancy:* The patients considered in this series may be divided into three groups according to the routine method of treatment in use at the time of admission. The first group, the earlier patients, 186 in number, were treated by large doses of alkalis, occasionally by acids and hexamine and only 4 (2.1%) patients had sterile urine during the pregnancy. The second group consisted of 37 patients—they were treated by ketogenic diet or by mandelic acid. 5 (13.5%) patients had sterile urine after treatment during pregnancy, although in many of the remaining 32 patients the growth of organisms was less profuse than it had been before treatment was given. The third group consists of the 64 patients treated by sulphonamides. In 36 (56.2%) of these the urine became sterile during pregnancy. The majority of these had sterile urine within one week of commencing treatment, the dosage varied between $7\frac{1}{2}$ to 15 grammes.

Dilatation of the pelvis of the kidneys and ureters is physiological in a high percentage in pregnancy. There were only two patients in the sulphonamide-treated group in whom there was no evidence of dilatation and in one of these the urine did not become sterile during pregnancy. On the other hand, there was no case with gross hydro-ureter or hydronephrosis in which the urine became sterile during pregnancy.

(c) *Risk of recurrence of acute infection during the pregnancy:* The only useful cases to be considered here are the 64 antenatal patients who were treated by sulphonamides. 7 of these patients were not readmitted to hospital for subsequent delivery and were therefore lost sight of. Of the remaining 57, 1 died, 3 had labour induced because they did not respond to treatment, 1 patient aborted, and two went into premature labour spontaneously during the first acute attack of pyelitis. Of the remaining 50 patients, only 4 had recurrent acute attacks of pyelitis; 3 of the 4 had had sterile urine after their first attack—the recurrence occurred in one patient ten weeks, in another twelve weeks and in the third, fourteen weeks after the primary attack. The fourth patient had been symptomatically cured but the urine still had organisms and pus cells. This patient had a recurrent acute attack six weeks after the initial attack.

The recurrence rate in this series was therefore 8%; recurrence may take place in the apparently cured as well as in the uncured. Hydro-ureter and hydronephrosis were present in the patients whose urine became sterile as well as in the patient whose urine did not become sterile.

(d) *Risk of recurrence in the puerperium:* 5 (10%) of the 50 patients treated by sulphonamides had an acute recurrence of infection in the early puerperium. The shortest interval between the initial attack and the recurrence was twelve weeks and the longest sixteen weeks. 3 of the patients were investigated and found to have hydro-ureter and hydronephrosis.

Effect of pyelitis on renal function in pregnancy.—Dilatation of the pelvis of the kidneys and ureters is physiological in pregnancy and is associated with delayed excretion of intravenous dyes and pyelography media. The dilatation and delayed excretion is generally more marked when there is associated infection, but this is not invariably so. 6 (9.2%) in the 64 sulphonamide-treated cases, 2 of whom had marked

hydronephrosis and hydro-ureter, developed a raised blood urea. None of these 6 patients had a previous history of renal disease.

(f) *Risk of associated late pregnancy toxæmia*: 73 of the 236 patients with antenatal pyelitis who were subsequently delivered in hospital of a viable foetus developed signs of toxæmia before the end of pregnancy; 2 had eclampsia. The incidence of toxæmia thus is 30·9%, while the incidence of toxæmia in 1,864 recent consecutive deliveries is 36%.

EFFECT ON FŒTUS.

Abortion		Less than 5½ lb.		Over 5½ lb.		Total
Spontaneous	Induced	Alive	Stillborn or died	Alive	Stillborn or died	
5	8	31	12	187	9	252

The foetal and neonatal mortality was 21 in 252 pregnancies = 8·3%.

38 of the 287 patients with antenatal pyelitis were not delivered in hospital. There were three sets of twins. 5 of the foetuses were grossly malformed.

Remote prognosis.—125 patients have been observed for periods of six months to fourteen years.

Subsequent pregnancies: 49 of the 125 have subsequently become pregnant; 3 of these are now pregnant with no evidence of recurrence so far. 27 (55·1%) patients had subsequent normal pregnancies; 25 had one normal pregnancy; 1 patient had two normal pregnancies, and another had 3 normal pregnancies.

Two patients had hypertension but no pyelitis in their subsequent pregnancies. One patient had pre-eclamptic toxæmia in the subsequent pregnancy. 16 (32·7%) patients had pyelitis in the immediately succeeding pregnancy. In 4 of the 16 there was also hypertension. 9 of the 16 became pregnant again; 4 of these had normal pregnancies—2 of the 4 had 2 further normal pregnancies. 5 of the 16 had a further pregnancy complicated by pyelitis. In the first recurrent pregnancy of 3 of these 5 patients there had been no hypertension but in all 3 patients in the further pregnancy there was hypertension in addition to pyelitis. In 2 of the 5 there was pyelitis and hypertension in the first recurrent pregnancy and this was present again in the succeeding pregnancy. All five patients showed evidence of renal impairment.

Remote prognosis in 76 patients who have not subsequently become pregnant: 40 (52·7%) have no evidence of pyelitis; 5 (6·5%) have chronic hypertension; 31 (40·7%) have chronic pyelitis, 7 of whom have also hypertension.

This is probably not a true picture as when we compare it with the history of the 49 patients who subsequently became pregnant 32 (61·5%) out of the 49 had eventually no evidence of pyelitis or kidney damage.

Professor J. Chassar Moir, Oxford: *Bladder injury following childbirth* [Abridged].—

1.—*Stress incontinence of urine*: Stress incontinence of urine, or incontinence on effort, as it is sometimes called, is one of the commonest of gynæcological symptoms; few women who have had a family are indeed quite free from this trouble. Almost without exception, incontinence is the result of the stretching of the vaginal walls and supports that takes place in childbirth.

Many attempts have been made to demonstrate by dissection a sphincter to the urinary bladder, without, so far as I am aware, any very convincing result—and this in spite of the fact that the bladder at its lower pole obviously has a sphincter action. This lack of an anatomical sphincter is, however, not so surprising as may at first appear, for the adjacent organ, the uterus, also lacks any clearly defined sphincter at its lower pole and yet is perfectly capable of retaining its contents during pregnancy in spite of the contractions that occur, more or less regularly, in the weeks before term. In both cases the signal for the emptying of the organ seems to be a relaxation of the interlacing fibres at the lower pole, together with, or in consequence of, persistent contractions of the musculature of the body.

The speaker then discussed reasons why the orthodox colporrhaphy type of operation on rare occasions failed to control stress incontinence, and described various operations that had been used in those resistant cases.

Finally, I wish to speak of the Goebell-Stoeckel operation and of its recent modification by Aldridge (1942) of New York.

In this operation a ribbon of fascia from the muscles of the anterior abdominal wall is dissected up on both sides; the upper ends are free but the lower ends are left attached to the pyramidalis muscle. A dissection is now made through the vagina on both sides of the upper urethra and a passage made to meet the abdominal dissection above (fig. 1). The two fascial ribbons are now brought down and united below the urethra to form a supporting sling for that organ. Finally, the vaginal dissection is closed as for a simple colporrhaphy.

I saw this operation performed by Werner in Vienna many years ago. I then thought it to be an unnecessary extensive and elaborate procedure; but I have since performed it myself in two resistant cases with a complete cure in the one case, and very satis-

an attack of shivering, occasionally with frequency of micturition, and still less often with vomiting. The acute stage lasts a few days in the majority of patients and thereafter with treatment the patient's general condition improves, the temperature subsides, the patient feels well and is symptomatically cured. The urine may or may not still be infected.

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The fœtal and neonatal mortality was 21 in 252 pregnancies = 8.3%.

38 of the 287 patients with antenatal pyelitis were not delivered in hospital. There were three sets of twins. 5 of the fœtuses were grossly malformed.

Remote prognosis.—125 patients have been observed for periods of six months to fourteen years.

Subsequent pregnancies: 49 of the 125 have subsequently become pregnant; 3 of these are now pregnant with no evidence of recurrence so far. 27 (55.1%) patients had subsequent normal pregnancies; 25 had one normal pregnancy; 1 patient had two normal pregnancies, and another had 3 normal pregnancies.

Two patients had hypertension but no pyelitis in their subsequent pregnancies. One patient had pre-eclamptic toxæmia in the subsequent pregnancy. 16 (32.7%) patients had pyelitis in the immediately succeeding pregnancy. In 4 of the 16 there was also hypertension. 9 of the 16 became pregnant again; 4 of these had normal pregnancies—2 of the 4 had 2 further normal pregnancies. 5 of the 16 had a further pregnancy complicated by pyelitis. In the first recurrent pregnancy of 3 of these 5 patients there had been no hypertension but in all 3 patients in the further pregnancy there was hypertension in addition to pyelitis. In 2 of the 5 there was pyelitis and hypertension in the first recurrent pregnancy and this was present again in the succeeding pregnancy. All five patients showed evidence of renal impairment.

Remote prognosis in 76 patients who have not subsequently become pregnant: 40 (52.7%) have no evidence of pyelitis; 5 (6.5%) have chronic hypertension; 31 (40.7%) have chronic pyelitis, 7 of whom have also hypertension.

This is probably not a true picture as when we compare it with the history of the 49 patients who subsequently became pregnant 32 (61.5%) out of the 49 had eventually no evidence of pyelitis or kidney damage.

Professor J. Chassar Moir, Oxford: *Bladder injury following childbirth* [Abridged].—*I.—Stress incontinence of urine:* Stress incontinence of urine, or incontinence on effort, as it is sometimes called, is one of the commonest of gynæcological symptoms; few women who have had a family are indeed quite free from this trouble. Almost without exception, incontinence is the result of the stretching of the vaginal walls and supports that takes place in childbirth.

Many attempts have been made to demonstrate by dissection a sphincter to the urinary bladder, without, so far as I am aware, any very convincing result—and this in spite of the fact that the bladder at its lower pole obviously has a sphincter action. This lack of an anatomical sphincter is, however, not so surprising as may at first appear, for the adjacent organ, the uterus, also lacks any clearly defined sphincter at its lower pole and yet is perfectly capable of retaining its contents during pregnancy in spite of the contractions that occur, more or less regularly, in the weeks before term. In both cases the signal for the emptying of the organ seems to be a relaxation of the interlacing fibres at the lower pole, together with, or in consequence of, persistent contractions of the musculature of the body.

The speaker then discussed reasons why the orthodox colporrhaphy type of operation on rare occasions failed to control stress incontinence, and described various operations that had been used in those resistant cases.

Finally, I wish to speak of the Goebell-Stoeckel operation and of its recent modification by Aldridge (1942) of New York.

In this operation a ribbon of fascia from the muscles of the anterior abdominal wall is dissected up on both sides; the upper ends are free but the lower ends are left attached to the pyramidalis muscle. A dissection is now made through the vagina on both sides of the upper urethra and a passage made to meet the abdominal dissection above (fig. 1). The two fascial ribbons are now brought down and united below the urethra to form a supporting sling for that organ. Finally, the vaginal dissection is closed as for a simple colporrhaphy.

I saw this operation performed by Werner in Vienna many years ago. I then thought it to be an unnecessary extensive and elaborate procedure; but I have since performed it myself in two resistant cases with a complete cure in the one case, and very satis-

factory result in the other. This latter patient I have had the honour to show to the meeting to-night. I think the most difficult part of the operation is to judge the correct tension to put on the sling. In my first case I made this too tight with the result that the patient had to have an indwelling catheter for nearly three weeks. In the second case I probably erred a little in the other direction.

II.—Vesico-vaginal fistula: I have elsewhere given an account of the extraordinarily interesting history connected with the treatment of this condition (Moir, 1940). To-night I can only recall that it was once one of the most dreaded of child-bed injuries. Sir J. Y. Simpson spoke of it as "the most depressing and deplorable of all the infirmities to which woman is liable, a condition looked upon as beyond all relief and hope". Although Marion Sims and others broke this conception, the vesico-vaginal fistula still retains more than a little of its sinister reputation. Why should this be so? I believe that it comes from a general lack of familiarity with this very special type of surgery which in this country, at least, is now seldom called for. Too often there is a tendency to regard the closure of a small hole as a form of minor surgery, and to engage in a hasty, ill-considered operation, without first investigating the special needs of the case. In these matters, Sims and his pupil Emmet have still much to teach us; and among modern workers I especially commend to your notice the works of George Gray Ward (1934, 1943), Phaneuf (1944), Miller (1935, 1942), Schmitz (1934) and Mahfouz (1929, 1934, 1938).

There are two forms of this injury after childbirth. The one is caused by operative trauma—for example, the unskilled use of the cranioclast; the other, by prolonged pressure of the foetal head. In this latter type urine may not escape until the lapse of eight or ten days when sloughing occurs. Occasionally, in a recent case, constant drainage by an indwelling catheter will allow spontaneous closure to take place (Dodds, 1941).

I believe that the vast majority of fistulae are curable, and further, that they are curable by vaginal operation. Let me quote from Mahfouz.

"For the last eight years I have not resorted to any of these abdominal operations; I find the vaginal route safer, and if I fail to close the fistula by the vaginal route I seldom succeed to do so by the abdominal."

These are the words of a man who speaks with the experience of 400 cases of vesico-vaginal fistulae, many of them of the most complicated nature, and many in patients riddled with bilharzial and other infections; of his last 100 reported cases 95% were cured.

I have read with disappointment certain recent publications in which the writers take such a gloomy view of the treatment of fistulae that they advocate, almost as a routine measure, the immediate transplantation of the ureters. No doubt good results can be obtained from this operation, but the cost is high. Mahfouz states: "Few patients survived the operation for more than three years." Murray and Ahmed writing of experience in India report that of 65 patients, 14 (21.5%) died after the operation. Roberts (1944) writing of experience in Nyasaland reports 90 cases with an average immediate mortality of 12.2%, although in 41 cases in which the Coffey No. 1 operation was performed in two stages there was only one death. Those last two reports do not include deaths that may have occurred from pyelonephritis after discharge from hospital. The overall mortality of the operation is therefore understated.

In fairness it should be stated that the authors just quoted were handicapped by working in tropical climates, and probably by many of their patients being ill-nourished and in poor general health. In temperate climates the operation of transplantation of ureters is rather less dangerous; and Henry Wade, Grey Turner, and others in this country have reported considerable success. Thus far, however, I have been unable to secure any considerable statistical evidence concerning the safety or otherwise of this operation when performed on healthy adult women.

To return now to the vaginal operation—which I firmly believe is applicable to almost every case of vesico-vaginal fistula—I would briefly list the essentials for success as follows.

(1) *Good exposure.*—An exaggerated lithotomy position is often sufficient, but in difficult cases the kneeling position suggested to me by Grey Turner, and shown in fig. 2 is the most helpful. Sometimes this must be combined with a generous episiotomy. A sucker is a great help in keeping the operation field free from blood and much to be preferred to the use of gauze swabs.

(2) *Excision of scar-tissue.*—Removal of scar-tissue must be free in order to allow healthy, oozing surfaces to be brought together. I do not regard the flap-splitting technique as being essential although I have occasionally used it.

(3) *Suture material.*—The suture material must be inert and non-irritating in order to avoid local exudate or reaction. Silk-worm gut, or nylon, may be used, but I prefer the silver-wire suture employed so successfully by Marion Sims and Emmet. Catgut should not be used save in cases in which infolding of a deep layer is obviously required:

even then, only two or three interrupted sutures of the finest chromicized catgut are permissible.

(4) *Absence of tension.*—Deep lateral incisions are sometimes required to relieve tension on the suture-line. These incisions may be left open to granulate. Sometimes a fibrous union to the pubic ramus must be divided.

(5) *Bladder drainage.*—The bladder should be kept absolutely empty by a catheter connected to a Bunsen-bottle apparatus to ensure constant gentle suction (fig. 3). A self-retaining catheter presses on the suture area and should therefore never be used. My own method is to place a silver-wire loop in the tissues immediately in front of the

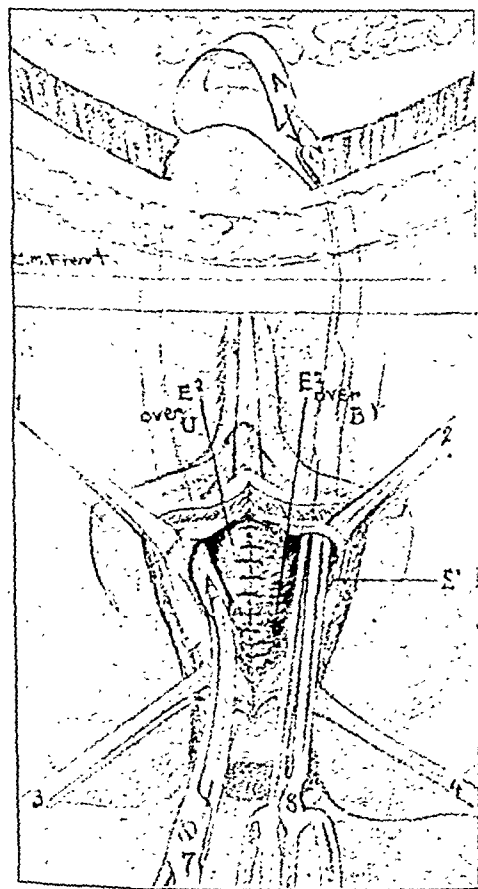


FIG. 1.—The Aldridge modification of the fascial sling operation. (Copied from "Transplantation of Fascia for Relief of Urinary Stress Incontinence," by A. H. Aldridge, *Amer. J. Obst. Gynec.*, 1942, 44, 407.)

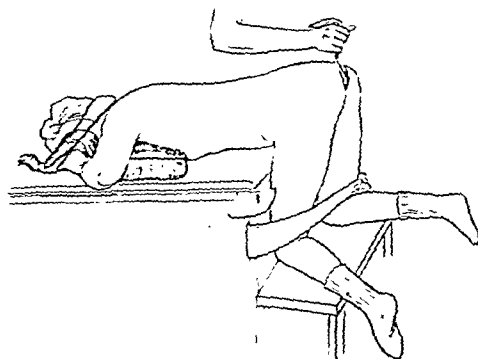


FIG. 2.—The kneeling position for use in vesico-vaginal fistula repair, when exposure is otherwise difficult.

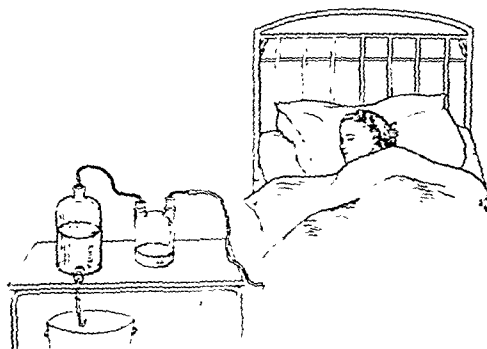


FIG. 3.—Post-operative drainage.

urethral meatus and to tie a plain catheter to this anchor. Drainage by a separate vaginal cystostomy is sometimes desirable (Moir, 1942).

(6) *Position after operation.*—In some cases it is an advantage to keep the patient face down, or substantially face down, for the first five or seven days after operation. The stitched area is then at a higher level than the rest of the bladder.

In this country, individual workers seldom see more than a few cases of vesico-vaginal fistula. I have been fortunate in being able to gather to the Nuffield Department in Oxford many such patients from various parts of the country. Even so, the numbers are necessarily small, and it seems almost an impertinence to quote them when workers such as Mahfouz can speak of 400 cases or more. My series includes, however, many of a very unusual nature. Excluding several vaginal cystotomies, there were 24 fistulae in 23 cases. In every case a closure was effected by a vaginal operation. For the present purpose gynecological are included with obstetric cases. One further successful case (one operation) might have been added, but as I have been unable to trace the notes I have omitted it from the list.

In many cases there had been multiple previous unsuccessful operations, some by the vaginal, some by the abdominal, and some by the transvesical routes. All the fistula cases save three were cured by one operation. The three exceptions were respectively: (1) A patient with seven previous operations, much scarring of the vagina, and fixation of the fistula to pubic bone; (2) a patient with eight previous operations, and most extensive scarring of the vagina; (3) a patient who had suffered a massive sloughing of the cervix, vagina, bladder, and to a lesser extent the anterior rectal wall, following radium therapy for carcinoma of the stump of the cervix. In each of these three cases the incontinence was cured by two operations. In the last case there was a separate operation on the rectum preceded by a temporary colostomy.

Two cases of complete absence of the urethra are listed separately. In those cases the urethra was reconstructed by the Ward technique. In each case a small secondary operation was later required. One of these patients now wears a pessary to press on the urethra and is completely relieved of incontinence. The other patient is improved, but the incontinence is not cured and she is still under observation with a view to further treatment.

From these figures I venture to say that the considerable pessimism sometimes voiced with regard to treatment is largely misplaced. Indeed, I believe that in the great majority of cases the vesico-vaginal fistula is an eminently curable lesion. Regarding operation, I have not yet encountered one which proved to be inaccessible by the vaginal route. Size is no contra-indication to operation; in one case I found an enormous opening with the bladder completely turned inside out into the vagina; repair was uneventful. Nor is prolonged duration of incontinence a contra-indication; in one of my patients incontinence had persisted for no less than twenty-eight years, yet this patient regained complete control of the bladder after repair. (Incidentally, it is calculated that this patient during her years of misery had washed more than 50,000 towels and had used at least 6,000 bales of cotton-wool!) Previous operation does, however, add greatly to the difficulty of subsequent closure. Here let me finish by a quotation from Schmitz:

"One of the greatest causes of failure in fistula operation must be attributed to the lack of understanding of the problem involved in the person who first failed to close the opening. The percentage of bad results mounts rapidly after each attempt at closure . . . The time to close the fistula is at the first sitting . . . and not after an unsuccessful attempt to close has seriously jeopardized the patient's chances of prompt and complete recovery."

(Case histories of the patients shown by Professor Chassar Moir will be found on page 662.)

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Mr. Howard G. Hanley: Gross urological pathology is present so frequently in pyelitis cases and can be masked so effectively by modern chemotherapy, that treatment directed towards the relief of symptoms and the lessening of the urinary infection is not enough. The development of pyelitis in a previously healthy urinary tract is a rare occurrence, so that a full urological examination should be carried out in every instance. The results of such an examination in 117 consecutive cases of pyelitis over a five year period are shown in Table I. 16% of the women suffered from some gross pathology such as double, ectopic or horseshoe kidneys, renal calculi, or gross pathological hydronephroses obviously present before the onset of the pregnancy.

TABLE I.—117 CONSECUTIVE CASES OF PYELITIS IN PREGNANCY

A	Congenital lesions	...	5%
B	Calculi	...	6%
C	Hydronephrosis	...	4%
D	Tuberculosis	...	1%
E	Combined gross pathology	...	16%
F	Previous genito-urinary infection	...	38%
G	Known previous pathology in urogenital tract before present attack	...	51%
H	Presence of urethro-trigonitis	...	39%
J	Cases with a possible primary causal factor within the genito-urinary system	...	55%

38% of the women gave a history of a previous urinary infection such as an attack of urethro-trigonitis, cystitis or pyelitis.

A marked degree of urethro-trigonitis was detected in 39% of the patients and the urethra is, I believe, a common source of latent urinary tract infection in the female.

I can support Miss Dodds' findings of the sudden onset of the pyelitis in many cases, but careful questioning revealed that over half of the patients suffered for a few days from increased frequency and dysuria before the onset of loin pain and pyrexia, &c.—i.e. clinically a urethro-trigonitis preceded the pyelitis.

Summarizing, there was evidence of a possible causal factor within the urogenital system in 55% of the cases.

More widespread use of the sulpha group of drugs by the general practitioner has reduced the admissions of pyelitis of pregnancy cases to hospital in spite of the great increase in the number of hospital deliveries. At the same time the severity of the disease has been greatly reduced since routine alkaline treatment was abandoned in favour of chemotherapy.

Mr. C. Keith Vartan: Pregnancy after transplantation of the ureters has not been mentioned by the previous speakers, and though it must be well known, it is unlikely that individual obstetricians will encounter many cases. Therefore I think it might help if I add to the discussion that I have recently been in a position to watch such a woman through her pregnancy. No urinary complication of any sort occurred, the end-result thus vindicating a refusal to terminate pregnancy on this score.

Mr. C. Scott Russell: *Rapid healing after vaginal cystotomy for calculus.*—As the discussion has turned to the use of vaginal drainage of the bladder in cases of vesico-vaginal fistula the following case record may be of interest.

Mrs. B., aged 30. Para. 3.—This patient reported to the Nuffield Department of Obstetrics & Gynaecology, Oxford, complaining of "bleeding whenever she went to the lavatory". Examination of the urine revealed a considerable hæmaturia, and cystoscopy and X-ray examination showed the presence of a foreign body in the bladder (it subsequently transpired that this was a piece of slippery elm bark which she had inserted—in error into the bladder—to procure an abortion at a time when incidentally she was not pregnant).

At Professor Moir's suggestion the bladder was opened through the anterior vaginal wall by cutting on to the tip of a tracheal dilator and the calculus was removed. Neither the opening in the bladder nor the cut in the vagina was sutured. A catheter was not inserted, though a small nylon stitch was put in the vestibule to which one could be tied should drainage later be required. The post-operative course is instructive in that despite the absence of suture there was only a slight vaginal leak of urine for the first twenty-four hours; thereafter she was quite dry and able to control her water and to pass it normally. The remainder of her convalescence was uneventful.

Reconstruction of a Completely Destroyed Urethra.—Professor J. CHASSAR MOIR, Oxford.

Mrs. C., aged 33, has had one baby. Five years ago, and six months after her confinement, she developed severe ulceration of the mouth and also of the vagina. Portions of tissue removed from the ulcer margins did not show any significant pathology. Frequent Wassermann tests were all negative. After a short time, the vaginal ulceration penetrated the bladder and she then suffered from complete incontinence of urine. Since then, the vaginal ulceration has slowly cleared up, but she still, from time to time, gets crops of ulcers in the mouth. During the past year this condition has been considerably relieved, but not altogether prevented, by administration of nicotinic acid, and later by nicotinamide.

Three attempts had been made to close the vesico-vaginal fistulæ, one of them by the abdominal route: they were all unsuccessful. When I first saw Mrs. C. there was a fistula, the size of a sixpence, opening straight into the bladder at a point that once marked the junction of bladder and urethra. There was then no trace of any urethra: that organ had completely disappeared, save for one or two small tags.

Using the G. G. Ward (1934) technique, a new urethra was constructed by dissecting up and forming a tube from the tissues of the vaginal wall between the fistula and cervix uteri. This tube was then turned over on its base and drawn through a new channel tunnelled below the structures that had previously carried the normal urethra. A vaginal cystotomy was then performed, and the bladder drained by a gentle suction. This operation was completely successful save for a tiny leak that later developed at the site of the "hinge". The latter opening was easily closed by a subsequent operation.

Mrs. C. was now provided with a new and functioning urethra; but, as might be supposed, considerable stress incontinence developed after she returned home and resumed activities. Following Ward's suggestion, a Hodge pessary was now fitted in the vagina, but in the upside-down position and with the rounded end directed for-

ward. This had the effect of keeping up a gentle pressure on the urethra while the patient was walking about. The result has been very successful. Mrs. C. is now quite dry by night, and is able by day to engage in all reasonable activities without any escape of urine. She has now been able to take up work as a secretary.

It is only right to add that I have had a second case of somewhat similar nature in which there was a complete absence of the urethra—the result, apparently, of a congenital abnormality. This patient has also been considerably improved by the reconstruction operation, but it has been difficult to get a pessary shaped to act as successfully as in Mrs. C.'s case. This latter patient is still under observation and will, I hope, be improved by later treatment.

REFERENCE

WARD, G. G. (1934) *Surg. Gynec. Obstet.*, 58, 67.

Repair of Vesico-vaginal Fistula: Incontinence Controlled by Fascial Graft.—Professor J. CHASSAR MOIR, Oxford.

Mrs. A. J. is a victim of the early air-raids on London. When near term she was evacuated to a distant county; and later, when two weeks post-mature, was admitted to a maternity home. She was four days in labour. The foetus died, and she was delivered by embryulcia. She became extremely ill—it is believed from a gas-forming infection—and for some time was not expected to recover. Some days later, massive sloughs came away from the vagina, and she became completely incontinent of urine. Although good general health was later regained, she has never since had a menstrual period. Subsequent examination *per vaginam* and *per rectum* failed to show anything suggestive of a uterine body or cervix. It seems that the entire organ had sloughed away, together with the anterior wall of the vagina and the upper part of the urethra. The left ureter could be seen spurting into the vagina. The right ureter was hidden behind folds of mucosa. At the upper end of the opening was a small mass of thicker tissue which may possibly have been the remains of a small portion of the anterior lip of the cervix.

Before she was referred to the Nuffield Gynaecological Department, Mrs. J. had had eight operations in an attempt to close the opening. Three of these were by the abdominal or transvesical route. In consequence, there was a vast amount of dense scar tissue around the fistula which enormously added to the difficulty of subsequent treatment.

Two operations of the Marion Sims's type (Moir, 1940) were required; the upper urethra was freed from the pubic bone, dense avascular scar tissue was excised, and the upper part of the opening was brought down to, and united with, the urethra. Anatomically, the fistula was now closed, but in consequence of the entire destruction of the sphincteric region, fistula-incontinence was replaced by urethral-incontinence. An operation to lengthen the urethra and to tighten the tissues around its upper part, did not bring about improvement. I therefore decided to perform the Goebell-Stoeckel operation in which a fascial sling from the anterior abdominal wall, with its base attached to the pyramidalis muscle, is brought down and united under the bladder neck to a similar sling from the other side. Aldridge (1942) of New York, has modified this operation, and his method has recently been favourably reported on by Studdiford (1944) and other American gynaecologists. In a previous case of somewhat similar nature I obtained an excellent result from this operation. In Mrs. J.'s case the extensive scarring of the abdominal wall prevented the formation of slings as recommended. I therefore secured strips of fascia from the thigh (in which operation I was kindly assisted by our surgical registrar, Mr. Cruickshank) and used them in a similar manner.

Substantial improvement has resulted from the operation. Mrs. J. is quite continent by night, and can now do her housework and shopping without difficulty. She can sit through a cinema performance without inconvenience, but agrees that with a long performance she would have to make a short absence.

One trouble continues in this case. Ever since the original obstetrical disaster Mrs. J. has from time to time had attacks of right-sided pain, sometimes associated with pyrexia, apparently caused by pyelitis. Pyelography shows both kidneys to be functioning, and not obviously abnormal. The ureteral opening on the right side, as seen by the cystoscope is, however, displaced and considerably wider than normal. The attacks yield to treatment with sulpha-drugs.

A difficulty in this type of operation is to judge the correct tension to put on the fascial slings. There is little margin between the too-tight and the too-slack position.

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Section of Ophthalmology

President—P. E. H. ADAMS, F.R.C.S.

[June 8, 1945]

Two Cases Showing Unusual Intra-ocular Foreign Bodies.—Major C. DEE SHAPLAND.

CASE I.—Sgt. E. J. was wounded on May 28, 1940, by bullet splash from an enemy machine gun on the armoured vehicle in which he was travelling on patrol. When hit he saw a flash in front of his face and felt pain in his left eye. He was taken to a R.A.P. where the injured eye was dressed, then to a field ambulance where the eye was again dressed and morphia and A.T.S. injections given. He was then transferred to a C.C.S. and while there was captured by the Germans. No further treatment was given, and the patient had to walk to another hospital some 18 kilometres away. A few days later he was transferred to a Belgian hospital. The left eye had been painful all this time. He was seen by a Belgian eye specialist on the afternoon of the day of his admission and drops were instilled. On the following day he was taken to the operating theatre, where, he understood, "lead was taken out of his eye." He later came under the care of a French eye specialist who stated that he could do nothing more for him, and on July 23, 1940, he was discharged from hospital and received no further treatment during his long period of captivity, although he was seen by a German eye specialist towards the end of 1940, who advised him to "wait until he got back to England." The patient stated that he had been "blind" in his left eye since the injury.

He was repatriated on May 11, 1945, and was first seen by Major Shapland at Millbank on May 23, 1945, being admitted to Shenley Military Hospital on the same day.

The left eye showed a divergent squint of some 10°, no active inflammatory signs and there was an anterior iritic synechia to a perforating corneal scar paracentrally at 7 o'clock. There were multiple, minute, glistening, metallic fragments on the iris and in the iris stroma, especially below, where there was a ragged, narrow, complete iridectomy; the eye was aphakic with dense capsule and there was no fundus reflex. The tension was normal and vision was reduced to perception of light with good projection. The right eye showed no abnormality and had standard vision unaided.

On May 24, 1945, the left eye was put up to a giant magnet with a negative result, and immediately afterwards the anterior synechia was divided with a Ziegler knife under local anaesthesia and at the same time a capsulotomy was performed. The eye settled down uneventfully from the operation, and its vision is now 6/12 with aphakic correction (+ 12.50 sph.)

The interest of this case was the fact that the injured eye, despite the presence of multiple non-magnetic metallic fragments on and in the iris stroma for five years showed no active inflammatory signs or evidence of degeneration resulting from chemical action. The nature of the intra-ocular metal must necessarily be a matter of speculation but was presumably derived from the German machine-gun bullet and therefore probably a lead-nickel alloy.

CASE II.—Capt. J. R. A. who on June 17, 1944, in Normandy, while examining a German underground cable by the roadside, pulled a piece of cord and an explosion occurred. He was taken to No. 21 F.D.S. with multiple wounds of the face and hands, and injuries to both eyes. He was transferred by ship to the Q. A. Hospital, Cosham, and was there until June 29, when he was moved to Park Prewett Hospital, Basingstoke, whence he was transferred on July 7, 1944, to the Military Hospital, Shaftesbury.

His face was much pitted and scarred from multiple fragments of stone of all sizes up to that of a large pea. The smaller fragments were quite superficial and were constantly being spontaneously extruded, the larger ones were deeper and were removed later from the mucous surface of both upper and lower lips, from the plane of the

ward. This had the effect of keeping up a gentle pressure on the urethra while the patient was walking about. The result has been very successful. Mrs. C. is now quite dry by night, and is able by day to engage in all reasonable activities without any escape of urine. She has now been able to take up work as a secretary.

It is only right to add that I have had a second case of somewhat similar nature in which there was a complete absence of the urethra—the result, apparently, of a congenital abnormality. This patient has also been considerably improved by the reconstruction operation, but it has been difficult to get a pessary shaped to act as successfully as in Mrs. C.'s case. This latter patient is still under observation and will, I hope, be improved by later treatment.

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Mrs. A. J. is a victim of the early air-raids on London. When near term she was evacuated to a distant county; and later, when two weeks post-mature, was admitted to a maternity home. She was four days in labour. The foetus died, and she was delivered by embryulcia. She became extremely ill—it is believed from a gas-forming infection—and for some time was not expected to recover. Some days later, massive sloughs came away from the vagina, and she became completely incontinent of urine. Although good general health was later regained, she has never since had a menstrual period. Subsequent examination *per vaginam* and *per rectum* failed to show anything suggestive of a uterine body or cervix. It seems that the entire organ had sloughed away, together with the anterior wall of the vagina and the upper part of the urethra. The left ureter could be seen spurting into the vagina. The right ureter was hidden behind folds of mucosa. At the upper end of the opening was a small mass of thicker tissue which may possibly have been the remains of a small portion of the anterior lip of the cervix.

Before she was referred to the Nuffield Gynaecological Department, Mrs. J. had had eight operations in an attempt to close the opening. Three of these were by the abdominal or transvesical route. In consequence, there was a vast amount of dense scar tissue around the fistula which enormously added to the difficulty of subsequent treatment.

Two operations of the Marion Sims's type (Moir, 1940) were required; the upper urethra was freed from the pubic bone, dense avascular scar tissue was excised, and the upper part of the opening was brought down to, and united with, the urethra. Anatomically, the fistula was now closed, but in consequence of the entire destruction of the sphincteric region, fistula-incontinence was replaced by urethral-incontinence. An operation to lengthen the urethra and to tighten the tissues around its upper part, did not bring about improvement. I therefore decided to perform the Goebell-Stoeckel operation in which a fascial sling from the anterior abdominal wall, with its base attached to the pyramidalis muscle, is brought down and united under the bladder neck to a similar sling from the other side. Aldridge (1942) of New York, has modified this operation, and his method has recently been favourably reported on by Studdiford (1944) and other American gynaecologists. In a previous case of somewhat similar nature I obtained an excellent result from this operation. In Mrs. J.'s case the extensive scarring of the abdominal wall prevented the formation of slings as recommended. I therefore secured strips of fascia from the thigh (in which operation I was kindly assisted by our surgical registrar, Mr. Cruickshank) and used them in a similar manner.

Substantial improvement has resulted from the operation. Mrs. J. is quite continent by night, and can now do her housework and shopping without difficulty. She can sit through a cinema performance without inconvenience, but agrees that with a long performance she would have to make a short absence.

One trouble continues in this case. Ever since the original obstetrical disaster Mrs. J. has from time to time had attacks of right-sided pain, sometimes associated with pyrexia, apparently caused by pyelitis. Pyelography shows both kidneys to be functioning, and not obviously abnormal. The ureteral opening on the right side, as seen by the cystoscope is, however, displaced and considerably wider than normal. The attacks yield to treatment with sulpha-drugs.

A difficulty in this type of operation is to judge the correct tension to put on the fascial slings. There is little margin between the too-right and the too-slack position.

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		Right	Left	Right	Left	Right	Left	Right	Left
1942									
Jan.									
Feb.			+		+				+
Mar.			0		0				0
Apr.									
May									
June									
July									
Aug.		+	+	+	+				
Sept.		0		0					
Oct.									
Nov.							+		+
Dec.									
1943									
Jan.			+		+		0		0
Feb.			0		0				
Mar.	Ephedrine		+		+		+		+
Apr.			+		+		+		+
May			+		+		+		+
June			+		+		+		+
July	Prostigmine		0		0		0		0
Aug.		+		+					
Sept.		0		0					
Oct.			+		+		+		+
Nov.			0		+		+		+
Dec.					+		+		+
1944									
Jan.			+		+		+		+
Feb.			+		+		0		+
Mar.	Treatment		0		0		+		+
Apr.	with		+		+		+		+
May	prostigmine		+		+		+		+
June	continued		+		+		+		+
July	during the		+		+		+		+
Aug.	year		+		+		+		+
Sept.			+		+		+		+
Oct.			+		+		+		+
Nov.			+		+		+		+
Dec.			+		+		+		+

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Female, aged 48. In 1935, after six months' treatment, she "left off taking thyroid because a sister, who was also taking thyroid, became a wreck". Eyes then became prominent and she received later deep X-ray treatment on account of "thyroid trouble" with marked success. She now complains that she is putting on weight and of puffiness under the eyes. There is absence of lid retraction; the presence of exophthalmos is indicated by the exposure of the sclera below the lower border of the iris. Some puffiness is present around both eyes. She shows obesity but otherwise her health remains good and she is able to earn her livelihood as a driver of a delivery van.

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The right eye was put on 1% atropine drops twice daily, the left on 1% atropine ointment with hot bathings every four hours and penicillin drops—500 units /c.c.—two-hourly by day. On July 9, 1944, the radiologist reported that there were no opaque intra-orbital foreign bodies right or left, and on the same day the left eye gave a negative response to the giant magnet. By July 18, the eyes had quietened sufficiently to remove several particles of stone embedded in the sclera and episclera of both eyes and on August 24, a drawing was made of the left eye by Sergeant E. R. Alexander. It shows quite well the multiple particles of stone embedded in the iris stroma (fig. 1).

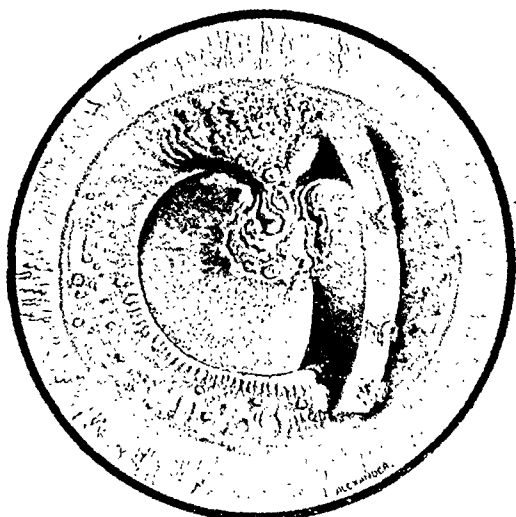


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1942									
Jan.									
Feb.			+		-				+
Mar.			O		O				O
Apr.									
May									
June									
July									
Aug.		+		-					
Sept.		O		O					
Oct.									
Nov.							+		+
Dec.									
1943									
Jan.			+		+				
Feb.			O		O		O		O
Mar.	Ephedrine		+		+		-		-
Apr.			+		+		-		-
May			+		+		-		-
June	Prostigmine		+		O		-		-
July		+	O	+			O		
Aug.		+		+					
Sept.		O	+	O	-				
Oct.			+		-				
Nov.			O		-		-		-
Dec.									
1944									
Jan.			+		+		+		+
Feb.			O		O		O		+
Mar.	Treatment		+		+		+		+
Apr.	with		+		+		+		+
May	prostigmine		+		+		+		+
June	continued		+		+		+		O
July	during the		+		+		+		
Aug.	year		+		+		+		
Sept.			+		+		+		
Oct.			+		+		+		
Nov.			+		+		+		
Dec.			+		+		+		

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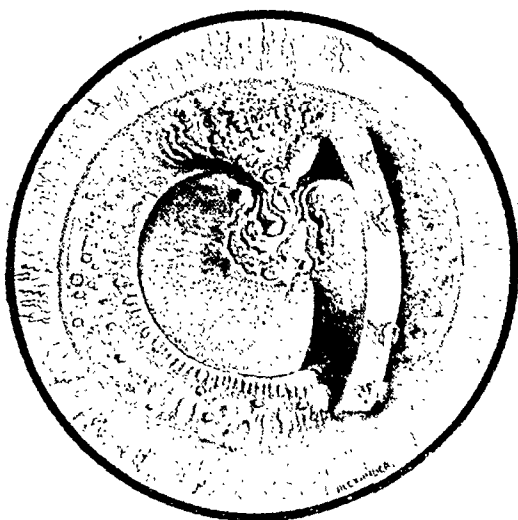


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1942									
Jan.			+		+				+
Feb.			0		0				0
Mar.									
Apr.									
May									
June									
July									
Aug.		+	+	+	+				
Sept.		0		0					
Oct.									
Nov.							+		+
Dec.									
1943									
Jan.			+		+		0		0
Feb.			0		0				
Mar.	Ephedrine	+	+	+	+	+	+	+	+
Apr.		+	+	+	+	+	+	+	+
May		+	+	+	+	+	+	+	+
June		+	+	+	+	+	+	+	+
July	Prostigmine	+	0	+	0	+	0	+	0
Aug.		+	+	+	+	+	+	+	+
Sept.		0	+	0	+	+	+	+	+
Oct.			+		+		+		+
Nov.			0		+		+		+
Dec.					+				
1944									
Jan.			+		+		+		+
Feb.			+		+		+		+
Mar.	Treatment		0		0		0		+
Apr.	with		+		+		+		+
May	prostigmine		+		+		+		+
June	continued		+		+		+		+
July	during the		+		+		+		+
Aug.	year		+		+		+		+
Sept.			+		+		+		+
Oct.			+		+		+		+
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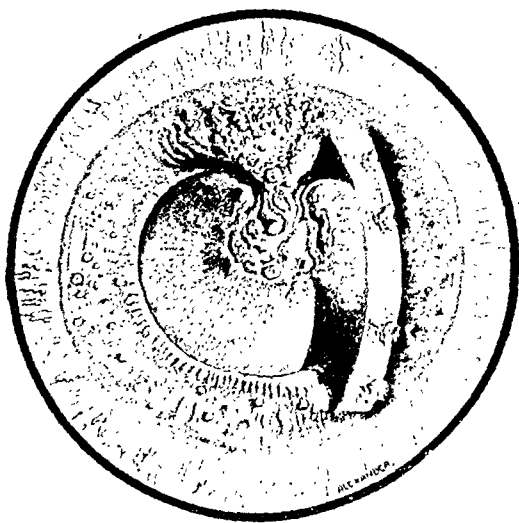


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improve the exophthalmos due to the thyrotropic hormone, by inhibiting the production of this hormone by the pituitary.

Since I published my earlier paper (Brain, 1937) I have seen 30 more cases, making 61 in all. The sexes are equally affected and the average age is 50. Out of 61 cases the condition followed thyroidectomy in only 11 and thiouracil in 1. In the post-thyroidectomy group males are affected at least four times as often as females. Since females get hyperthyroidism nine times as often as males, males are 36 times more likely than females to get exophthalmic ophthalmoplegia after thyroidectomy for thyrotoxicosis. This striking sex difference seems to favour an endocrine factor in aetiology rather than mere increase in weight or myxoedema.

For treatment I have chiefly used œstrin for both sexes. The results are mostly disappointing, occasionally very good. Most patients improve up to a point. I have increased the dose up to 20 mg. of stilbæstrol daily in some cases.

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It therefore seems likely that clinically we should be able to distinguish these various primary and secondary effects of excess pituitary thyrotropic hormone from the effects of excess thyroxine and possibly coincident excess adrenaline acting on thyroxine-sensitized structures, or against thyroxine-weakened antagonists. We are looking for three sets of eye signs, namely, signs of overaction of unstriated muscle (lid retraction and exophthalmos abolished by anaesthesia), signs of weakness of striated muscle (ophthalmoplegia), and signs of increase in bulk (water retention) in the orbital and lid tissues (proptosis, chemosis and oedema of lids). General changes due to excess or

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There is now considerable evidence in favour of thyrotoxic exophthalmos and ophthalmoplegia, however thyrotoxicosis may operate. In addition to the work I have quoted, there is some evidence that exophthalmos may be produced by the administration of thyroid extract and disappear on its withdrawal (Brain, 1936). There is also the improvement in both exophthalmos and ophthalmoplegia which sometimes follows thyroidectomy, or the administration of thiouracil. But neither exophthalmos nor ophthalmoplegia is usually severe in thyrotoxicosis except perhaps in older patients.

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improve the exophthalmos due to the thyrotropic hormone, by inhibiting the production of this hormone by the pituitary.

Since I published my earlier paper (Brain, 1937) I have seen 30 more cases, making 61 in all. The sexes are equally affected and the average age is 50. Out of 61 cases the condition followed thyroidectomy in only 11 and thiouracil in 1. In the post-thyroidectomy group males are affected at least four times as often as females. Since females get hyperthyroidism nine times as often as males, males are 36 times more likely than females to get exophthalmic ophthalmoplegia after thyroidectomy for thyrotoxicosis. This striking sex difference seems to favour an endocrine factor in aetiology rather than mere increase in weight or myxœdema.

For treatment I have chiefly used œstrin for both sexes. The results are mostly disappointing, occasionally very good. Most patients improve up to a point. I have increased the dose up to 20 mg. of stilbœstrol daily in some cases.

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The main line of treatment of all these groups was to raise the B.M.R. with thyroid extract in those cases in which it was low. This was combined with tarsorrhaphy and plastic operations on the lids and conjunctiva where necessary. In no case was orbital decompression required. In cases with a raised B.M.R. from the beginning, treatment was individual, in some deep X-ray therapy to the pituitary, in others, sedatives and rest. One case benefited from testosterone.

Dr. S. Leonard Simpson said that Dr. Russell Brain, in opening the discussion, had referred to the fundamental work which had been done on this subject. Not a little of that work had been done by Dr. Brain himself. On the present occasion they had had the addition of some valuable clinical material by Professor Ida Mann.

He would like for a moment to depart from a close view of the end-results of illness, and urge how very much might be done by a prophylactic psychiatric approach to the problem. Anxiety and shock played an aetiological part both in thyrotoxicosis and in exophthalmic ophthalmoplegia. This was also true of duodenal ulcer, effort syndrome (D.A.H.) and some forms of hypertension, from which it appeared that the nature of the derangement depended very much upon which organs or tissues of an individual were susceptible to the stimuli which came from the hypothalamus and perhaps from the pituitary. Were we not looking at the end-results of a psychogenic-hypothalamic syndrome?

Experimental evidence indicated that the thyrotropic hormone alone produced exophthalmos, and although thyroxine might augment this effect, he did not believe that thyroxine alone could produce exophthalmos in man as distinct from lid retraction. Theoretically, withdrawal of thyroxine could, as a release phenomenon, produce the secretion of thyrotropic hormone but he had seen many hundreds of cases of people who had had very large doses of thyroxine, producing sweating and tachycardia, and he had never himself seen—although a few cases had been reported—exophthalmos of any severity produced by thyroxine alone.

Concerning the group which Dr. Brain had separated—and quite clearly it looked a different clinical group—one must remember that the ophthalmoplegia was not necessarily present in the early part of the syndrome, so that there was a gradual transition from exophthalmos to exophthalmic ophthalmoplegia. The group looked different, the age was different, and the sex incidence (predominantly male) was different.

The theory he would suggest was the following. If it was accepted that the pituitary thyrotropic hormone produced exophthalmos, both in Graves' disease and in the exophthalmic ophthalmoplegic group, in the latter the thyroid was incapable of responding to the thyrotropic hormone. This was not improbable on clinical grounds. First of all there was the age of the patients to be taken into consideration—round about 50—and although one could get Graves' disease in old people it was much rarer and then again, in the bulk of the cases were in men, in whom the thyroid was much less labile than in women. The theory could be put to the test by injecting these people with thyrotropic hormone, and seeing if a raising of the B.M.R. was produced. The theory certainly appeared to apply to that type of exophthalmic ophthalmoplegia which followed extensive thyroidectomy, and which was associated with a low metabolic rate.

It was recognized clinically that toxic adenoma as distinct from Graves' disease was associated with minimal eye change, and rarely recurred after thyroidectomy. The reason for that would be that in the toxic adenomas it was not the thyrotropic hormone that was operating, but the primary activity of the thyroid gland. This was quite comparable with other endocrine diseases. Thus one might have either a single non-recurrent cystic ovary, or multiple cystic ovaries which regenerated after taking out one ovary and part of the other. The same held good for the adrenal glands.

He thought that testosterone was more logical for use in men than oestradiol, which was more logical in women. Testosterone was as likely to inhibit the pituitary as was oestradiol, and massive oestradiol therapy was associated with retention of fluid. Neither hormones nor deep pituitary radiation could produce satisfactory results where irreversible secondary changes had taken place in the orbit.

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Mr. E. E. Pochin referred to some of the quantitative data that he had obtained with Mr. Rundle. They had examined a series of 17 cases of thyrotoxicosis coming to post-mortem, including six diagnosed as having exophthalmos, and had made a complete removal and analysis of the orbital contents. Where present, the exophthalmos had been of the simple type common in Graves' disease and not the so-called "malignant" or severe form.

deficiency of thyroxine (raised or lowered B.M.R. and loss or gain in weight), may also complicate the picture. In addition, in man, we are confronted by the possible action of the central nervous system acting through the hypothalamic structures as the stimulant or depressor of the pituitary gland. This aspect must always be borne in mind. Its importance was pointed out by Russell Brain in 1936, when he stated that in the majority of his patients with exophthalmic ophthalmoplegia there was a history of mental shock or emotional strain from extrinsic causes. Purely psychogenic sources of emotional disturbances were conspicuously absent.

Eighteen cases are described on the presumptive evidence of the probable single or multiple endocrine disturbances underlying them. Pure thyrotoxic cases have not been included, as the problem has been tackled chiefly from the pituitary point of view.

The cases seem to fall into three groups:

Group I.—Primary deficiency of thyroxine with compensatory excess of thyrotropic hormone secretion (4 cases).

Group II.—Primary excess thyroxine as initial symptom followed by thyroid atrophy or removal, replaced by excess thyrotropic hormone (10 cases).

Group III.—Excess thyroxine and excess thyrotropic hormone arising simultaneously (4 cases).

Group I.—Primary thyroxine deficiency with compensatory excess thyrotropic hormone: Three women and one man fall into this group. They are all between 50 and 60 (average 54) years. One patient gave a history of fright in an air raid and one of overwork. The other two could assign no cause and were not neurotic personalities. In all four patients there was oedema of the lids and, in three, of the conjunctiva also. The lids appeared puffy, stiff and showed poor movement. In three cases the lids could not be completely closed, but lid retraction was not present and the appearance did not suggest thyrotoxicosis. The patients' skin was sallow, thick and coarse, and slightly suggestive of myxoedema. The proptosis (in three) could not be reduced by pressure and the B.M.R. in the three cases in which it is known was subnormal (-9% , -27% and 0 to -1%). In two of the cases one eye was lost from exposure before I saw the patient, but the other eye was saved by tarsorrhaphy and excision of conjunctiva, the patient being put on to thyroid extract until the B.M.R. was well raised. One case was seen very early and required no local treatment. The fourth case had partial tarsorrhaphy and her eyes were saved, though she showed many anomalous features and her early history is obscure.

Group II.—Cases in which the presenting symptoms suggest excess thyroxine followed by thyroid failure, or thyroidectomy, and subsequent excess thyrotropic hormone: Ten cases fall into this group, eight are women and two men. Their ages range from 44 to 76, distributed thus, 44, 47 (2), 54, 56, 57, 60, 62, 71, 76. In seven cases there is a definite history of shock or mental strain followed by symptoms of hyperthyroidism. In three there was no history other than the usual complaint of overwork and war anxiety. Of the seven cases giving a definite history, the shock was in five connected with the war; personal experience in air raids (2), death or injury of near relation (2), hardship over billetes (1). The sixth case was that of personal worry over a criminal member of the family and the seventh the shock of an operation for strangulated hernia. In two of these cases there was a previous breakdown with tachycardia and loss of weight following in one case a motor smash and in the other the death of a husband. In them all the history was of an illness characterized by loss of weight and tachycardia, followed either by recovery or thyroidectomy. Swelling of the lids, proptosis and ophthalmoplegia then developed, sometimes after a second shock, sometimes independently. Six of the ten cases had had thyroidectomy with improvement, immediate, but not maintained. The time elapsing between the thyroidectomy or the spontaneous remission of the tachycardia and the appearance of the ophthalmoplegia varied from 14+ years in two cases with history of second shock, to a few days in some of the thyroidectomized cases.

Group III.—Excess thyroxine and excess thyrotropic hormone arising simultaneously: Four cases fall into this group, three men and one woman, aged respectively 42, 53 and 60 (2). Two gave history of war experiences (shipwreck and bombing) and two of overwork in civilian life. In all four the symptoms were loss of weight, tachycardia, proptosis and ophthalmoplegia all coexistent, the loss of weight slightly preceding the exophthalmos in two cases. The B.M.R. in three was high ($+38\%$, $+42\%$, and $+43\%$), in the fourth it was not taken before treatment. On this account they could not be given thyroid extract and were all treated differently on their individual merits.

Section of Psychiatry

President—A. F. TREDGOLD, M.D.

[May 24, 1945]

DISCUSSION ON BIOCHEMISTRY AND PSYCHIATRY

Mr. G. D. Greville: *Recent developments [Abridged].*—The hippuric acid excretion test in schizophrenia.—Quastel and Wales (1938, 1940), using Quick's oral test, found that all their catatonics, but only 15% of the schizophrenics of other types, showed an abnormally low hippuric acid excretion, i.e. one corresponding to 2.9 g. or less of benzoic acid. We (Ström-Olsen, Greville and Lennon, 1938) were unable to confirm this difference between catatonics and other schizophrenics, but two other groups of workers were in partial agreement with Quastel and Wales (see table). Finkelman

	Average hippuric acid excretion in 4 hrs. (as benzoic acid)		Patients with excretion equal to or less than 2.9 g.		Number of patients examined	
	C	NC	C	NC	C	NC
Quastel and Wales (1938)	2.2	3.4	100%	15%	18	27
Ström-Olsen <i>et al.</i> (1938)	3.3	3.5	18%	18%	28	34
Finkelman <i>et al.</i> (1940)	2.9	3.7	47%	11%	17	9
Quastel and Wales (1940)	2.1	—	100%	—	12	—
Davies and Hughes (1940)	2.7	2.9	88%	54%	17	28

C: catatonics NC: other schizophrenics

suggested that low values in catatonia might result from the immobility of the muscles. Hippuric acid synthesis is now known to be dependent on body-weight (Scurry and Field, 1943). The disagreement between Quastel and Wales and ourselves does not, however, result from neglect of the patients' weights. For if a scatter diagram is plotted from our own data, the points for the two groups of patients are intermingled (fig. 2); from Quastel and Wales's data, the two groups are separate (fig. 1). Nevertheless it would be well to take account of body-weight in future work, for all the non-catatonic patients with excretions below 2.9 g. are of light weight (figs. 1 and 2).

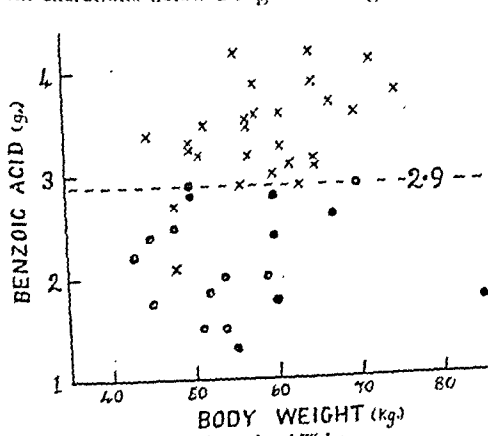


FIG. 1.—Quastel and Wales.
● Catatonics.

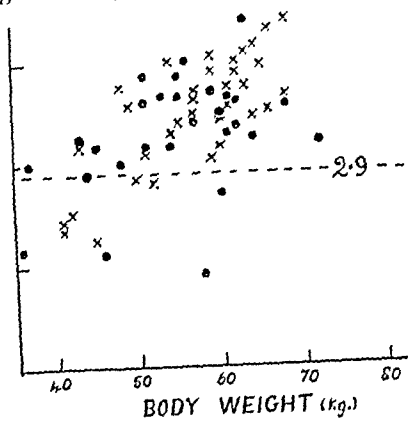


FIG. 2.—Ström-Olsen *et al.*
● Catatonics. / Other schizophrenics.

Michael, Looney and Borkovic (1944) do indeed record the excretion as mg. sodium benzoate per kg. body-weight. They find the following average values after giving 80 mg. sodium benzoate per kg. by mouth: For 9 controls, 59; 4 catatonics, 59, 15 other schizophrenics, 60. In the same units, the average for Quastel and Wales's catatonics is 47, and their other schizophrenics 68.5; for our catatonics 72, and other schizophrenics 72.5. I cannot explain the discrepancy between our results and those of Quastel and Wales.

Spontaneous hypoglycæmia.—In addition to spontaneous hypoglycæmia with a clear organic basis, there exists the so-called "functional hypoglycæmia" (see Wauchope, 1933). This may be acute or chronic; complete recovery is possible; and the aetiology is indefinite, although there may be a hereditary component (Cambridge, 1930). It is

It was found that the bulk of the orbital tissues was increased by an amount corresponding to the displacement of the eye observed in these cases [1]. The increase was due to an excess of fat in the orbital structures, affecting particularly the skeletal eye muscles in which this ether extract component was more than doubled. It was of significance that this change in the eye muscles was found in 15 of the 17 cases and not merely in those with exophthalmos.

In the light of these findings, what was the probable relationship between simple and "malignant" exophthalmos? The distinction between these types had developed at a time when it was thought that simple exophthalmos was not associated with increase in orbital bulk, enlargement of the eye muscles, or ophthalmoplegia, whereas "malignant" exophthalmos was known to exhibit these features. It had now been shown that in simple exophthalmos orbital tissues and particularly muscles were increased in bulk. In addition the careful work of Rundle and Wilson on ophthalmoplegia in thyrotoxic subjects [2], which his own measurements fully supported, showed limitation of ocular movement also to be frequent in simple exophthalmos. It thus appeared that each of these phenomena occurred in mild degree in mild or simple exophthalmos, and more severely in severe or "malignant" exophthalmos. Was "malignant" exophthalmos merely a more advanced, and secondarily complicated stage of simple exophthalmos?

He would suggest one hypothesis which was very far from being proved but which might provoke investigation. It was possible that, as orbital tissue bulk increased in simple exophthalmos, a stage of severity was reached at which the vascular drainage of the orbit was mechanically impeded. The added orbital bulk so caused then started the rapid progression of malignant exophthalmos with its severe protrusion, clinical evidence of congestion, and post-mortem findings of œdema and later fibrosis. On this view it seemed likely that any rapid gain in body-weight, such as might follow thyroidectomy, could in an exophthalmic subject increase the bulk of the orbital tissues enough to tip the scale and precipitate the progressive changes of "malignant" exophthalmos.

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Professor Ida Mann, in reply, said that orbital decompression had not been done in any of her series. She knew that Mulvany had stated that if one had to deal with the malignant type one must perform Naffziger's operation to save the eye, but she thought she had shown that tarsorrhaphy plus the administration of thyroid extract did save the eye without this. Orbital decompression was, of course, a grave operation whereas tarsorrhaphy was not, and in any case with proper endocrine treatment the condition should subside and the large mutilating operation of removing the orbital roof should not be necessary.

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DISCUSSION ON BIOCHEMISTRY AND PSYCHIATRY

Mr. G. D. Greville: *Recent developments [Abridged].—The hippuric acid excretion test in schizophrenia.*—Quastel and Wales (1938, 1940), using Quick's oral test, found that all their catatonics, but only 15% of the schizophrenics of other types, showed an abnormally low hippuric acid excretion, i.e. one corresponding to 2.9 g. or less of benzoic acid. We (Ström-Olsen, Greville and Lennon, 1938) were unable to confirm this difference between catatonics and other schizophrenics, but two other groups of workers were in partial agreement with Quastel and Wales (see table). Finkelman

		Average hippuric acid excretion in 4 hrs. (as benzoic acid)		Patients with excretion equal to or less than 2.9 g.		Number of patients examined	
		C	NC	C	NC	C	NC
Quastel and Wales (1938)	...	2.2	3.4	100%	15%	18	27
Ström-Olsen <i>et al.</i> (1938)	...	3.3	3.5	18%	18%	28	34
Finkelman <i>et al.</i> (1940)	...	2.9	3.7	47%	11%	17	9
Quastel and Wales (1940)	...	2.1	—	100%	—	12	—
Davies and Hughes (1940)	...	2.7	2.9	88%	54%	17	28
		C: catatonics		NC: other schizophrenics			

suggested that low values in catatonia might result from the immobility of the muscles.

Hippuric acid synthesis is now known to be dependent on body-weight (Scurry and Field, 1943). The disagreement between Quastel and Wales and ourselves does not, however, result from neglect of the patients' weights. For if a scatter diagram is plotted from our own data, the points for the two groups of patients are intermingled (fig. 2); from Quastel and Wales's data, the two groups are separate (fig. 1). Nevertheless it would be well to take account of body-weight in future work, for all the non-catatonic patients with excretions below 2.9 g. are of light weight (figs. 1 and 2).

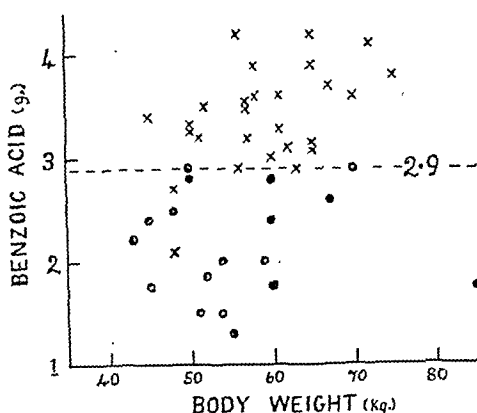


FIG. 1.—Quastel and Wales.

● Catatonics.

× Other schizophrenics.

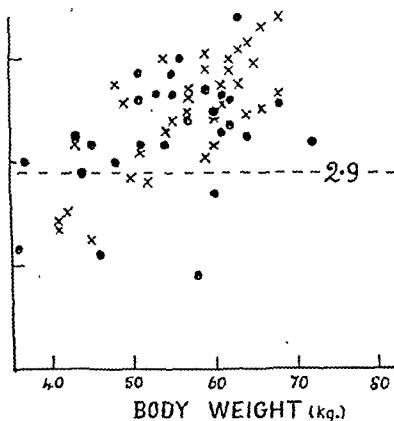


FIG. 2.—Ström-Olsen *et al.*

Michael, Looney and Borkovic (1944) do indeed record the excretion as mg. sodium benzoate per kg. body-weight. They find the following average values after giving 80 mg. sodium benzoate per kg. by mouth: For 9 controls, 59; 4 catatonics, 59; 15 other schizophrenics, 60. In the same units, the average for Quastel and Wales's catatonics is 47, and their other schizophrenics 68.5; for our catatonics 72, and other schizophrenics 72.5. I cannot explain the discrepancy between our results and those of Quastel and Wales.

Spontaneous hypoglycæmia.—In addition to spontaneous hypoglycæmia with a clear organic basis, there exists the so-called "functional hypoglycæmia" (see Wauchope, 1933). This may be acute or chronic; complete recovery is possible; and the aetiology is indefinite, although there may be a hereditary component (Cambridge, 1930). It is

It was found that the bulk of the orbital tissues was increased by an amount corresponding to the displacement of the eye observed in these cases [1]. The increase was due to an excess of fat in the orbital structures, affecting particularly the skeletal eye muscles in which this ether extract component was more than doubled. It was of significance that this change in the eye muscles was found in 15 of the 17 cases and not merely in those with exophthalmos.

In the light of these findings, what was the probable relationship between simple and "malignant" exophthalmos? The distinction between these types had developed at a time when it was thought that simple exophthalmos was not associated with increase in orbital bulk, enlargement of the eye muscles, or ophthalmoplegia, whereas "malignant" exophthalmos was known to exhibit these features. It had now been shown that in simple exophthalmos orbital tissues and particularly muscles were increased in bulk. In addition the careful work of Rundle and Wilson on ophthalmoplegia in thyrotoxic subjects [2], which his own measurements fully supported, showed limitation of ocular movement also to be frequent in simple exophthalmos. It thus appeared that each of these phenomena occurred in mild degree in mild or simple exophthalmos, and more severely in severe or "malignant" exophthalmos. Was "malignant" exophthalmos merely a more advanced, and secondarily complicated stage of simple exophthalmos?

He would suggest one hypothesis which was very far from being proved but which might provoke investigation. It was possible that, as orbital tissue bulk increased in simple exophthalmos, a stage of severity was reached at which the vascular drainage of the orbit was mechanically impeded. The added orbital bulk so caused then started the rapid progression of malignant exophthalmos with its severe protrusion, clinical evidence of congestion, and post-mortem findings of œdema and later fibrosis. On this view it seemed likely that any rapid gain in body-weight, such as might follow thyroidectomy, could in an exophthalmic subject increase the bulk of the orbital tissues enough to tip the scale and precipitate the progressive changes of "malignant" exophthalmos.

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- 1 RUNDLE, F. F. and POCHIN, E. E. (1944), *Clin. Sci.*, 5, 51.
- 2 ——— and WILSON, C. W. (1944), *Clin. Sci.*, 5, 17.

Professor Ida Mann, in reply, said that orbital decompression had not been done in any of her series. She knew that Mulvany had stated that if one had to deal with the malignant type one must perform Naffziger's operation to save the eye, but she thought she had shown that tarsorrhaphy plus the administration of thyroid extract did save the eye without this. Orbital decompression was, of course, a grave operation whereas tarsorrhaphy was not, and in any case with proper endocrine treatment the condition should subside and the large mutilating operation of removing the orbital roof should not be necessary.

The considerable day-to-day variations in O.G.T. observed even in normal subjects (see for example Freeman, Looney and Hoskins, 1942) do not, as might seem likely, invalidate the work on melancholia. They probably result from delays in glucose absorption, and reduce the usefulness of the O.G.T. curve in measuring utilization and hence in the diagnosis of diabetes. In psychiatric work, however, as we have seen, such variations should be regarded with interest rather than deprecation.

Brain metabolism.—The oxygen consumption of the brain is measured in man by determining the oxygen contents of blood from an artery and from the internal jugular vein. The difference between these—the arterio-venous (A.-V.) difference—if multiplied by the rate of blood-flow, gives the oxygen consumption. The difficulty lies in the measurement of blood-flow. The thermo-electric needle (Gibbs, 1933) will indicate changes in flow in a vessel, but gives no absolute values. In the "plethysmographic" method (Ferris, 1941) the rate of displacement of C.S.F. through a lumbar-puncture needle when the venous return is obstructed by inflation of a cuff round the neck is taken as representing the arterial inflow. The method lays itself open to criticism both from physiologists (Gregg and Shipley, 1944) and, one would imagine, from the subjects; but it is the only one which gives any figure for the intracranial blood-flow in man.

The following table shows that brain A.-V. differences are not abnormal in schizophrenia:

	Subjects	Average brain A.-V. differences			Authors
		Oxygen (vols. %)	CO ₂ (vols. %)	Glucose (mg. per 100 ml.)	
50 normal young men	...	6.7	6.6	9.8	Gibbs <i>et al.</i> (1942)
23 hospitalized controls	...	6.9	6.4	9	Wortis <i>et al.</i> (1940)
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Rosenbaum, Roseman, Aring and Ferris (1942) found by the plethysmographic method values from 105 to 170 (average 131) ml. per min. for intracranial blood-flow in normal subjects, and from 87 to 162 (average 117) in schizophrenics. It therefore seems likely that gross cerebral metabolism is normal in schizophrenia, although some simultaneous measurements of A.-V. difference and blood-flow ought to be made.

Himwich and Fazekas (1944a) from A.-V. difference measurements consider that cerebral metabolic rate is normal in adult undifferentiated mental defectives, but reduced in mongolism, cretinism, phenylpyruvic oligophrenia, advanced hydrocephalus, microcephaly and amaurotic familial idiocy. The same authors (1944b) have determined A.-V. differences in pernicious anaemia, cardiac failure and luetic encephalitis, with interesting results.

Changes in cerebral metabolism during "shock" therapy have been much studied, especially by Himwich, Loman, Wortis and their colleagues. The expected reduction in cerebral oxygen—and glucose—uptake during insulin hypoglycaemia has been duly established: the A.-V. differences are reduced, with negligible change in the rate of blood-flow, as determined by both Gibbs's and Ferris's methods. During leptazol convulsions, on the other hand, there is increase in blood-flow, which makes it difficult to establish that there is reduced oxygen-uptake during the period of hypoxia; this, however, is highly probable. Davis, McCulloch and Roseman (1944), using an ingenious electrical method, have found that induced seizures in cats are accompanied by a fall in the oxygen-tension of the cortex, which begins several seconds before the fit; this they ascribe to an increase in cerebral metabolism provoked by the exciting agent.

Belief that reduced cerebral respiration was the factor common to the various "shock" therapies led Alexander and Himwich (1939) to try partial asphyxiation by nitrogen as a treatment of schizophrenia. Several other workers have subsequently tried this, with promising initial results but ultimate disappointment. Surely, however, insulin and convulsion therapies are not equally effective in the treatment of schizophrenia; and the effect of short sharp hypoxia were better tested on the affective psychoses, where convulsion therapy is more successful.

In conclusion, the biochemists want help from clinical research officers, who with the Medical Director will integrate the clinical side, choosing the patients and following their subsequent progress for years if need be. For metabolic studies we need research wards, with adequate and highly conscientious nursing staff.

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The reciprocal relationship between hypoglycaemia and mental state is well shown in a small group of cases, described by Rennie and Howard (1942), presenting the syndrome "tension-depression with hypoglycaemia". In this, hypoglycaemic episodes occur *after* food, with symptoms which may be alarming, and the oral glucose tolerance curves are flat. After treatment of the psychiatric disorder, the episodes fail to appear, and the tolerance curves return to 'normal'. The authors suggest that the fault lies in the mechanism which calls a halt to net glycogen storage, and that the treatment of certain cases of hypoglycaemia should be focused on the personality disturbance.

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The oral glucose tolerance test in melancholia.—Although previous workers had observed abnormal oral glucose tolerance (O.G.T.) in depression, ideas were systematized by McCowan and Quastel (1931) who introduced the hyperglycaemic index (H.I.). This is given by the fraction:

$$\frac{\text{Two-hour blood-sugar level} - \text{fasting level}}{\text{Maximum blood-sugar level} - \text{fasting level}} \times 100$$

It is a measure of prolongation of hyperglycaemia, the curve of most abnormal shape having an H.I. of 100. When 50 g. of glucose are given, an H.I. of 0 to 10 is considered normal. McCowan and Quastel found the closest parallelism between H.I. and emotional tension. A normal H.I. in a case of melancholia indicated a hysterical element, with bad prognosis. The H.I. was also a guide to progress, falling from a high to a low value on recovery. Some subsequent authors were less sanguine about the agreement between H.I. and observed mental state. I can give no opinion. I should like, however, to discuss the cause of the O.G.T. abnormality so often found.

Two types of abnormal curve occur in melancholia, the flat curve and the high curve with delayed return, both starting from a normal or even subnormal fasting level. I do not think that these types are of fundamentally different causation, for when in 1940 Dr. D. Russell Davis and I studied depressed patients kept under controlled conditions and on a fixed carbohydrate intake, the curves switched from one shape to the other, without significant change in mental state.

The O.G.T. curve is determined by the varying rates of absorption and utilization of glucose. A measure of the utilization may be given by the intravenous glucose tolerance. Gildea, McLean and Man (1943), working with manic-depressives, obtained both oral and intravenous curves. Finding that the latter were normal by the standards which they adopted, they concluded that the abnormality of the former arose from delayed absorption rather than faulty utilization. The evidence was incomplete, since most of their O.G.T. curves were not very abnormal, and also variations in intravenous tolerance, within their generous limits of normality, might still represent one factor affecting the shape of the oral curve. Indeed, the apparent lack of correlation between oral and intravenous tests might result from their necessarily crude method of assessing the latter. The intravenous curve conforms closely to an exponential equation containing three constants (Greville, 1943), and the need for three constants renders the evaluation of the curve very difficult.

The unpublished work with Dr. Russell Davis to which I have referred, however, gives evidence in support of Gildea and his colleagues. Following a suggestion by Mr. T. C. Hall, we found that in the O.G.T. curves of depressed patients there is correlation between the average slope over the first thirty minutes and the H.I., that is, the lower the initial rate of rise of blood-sugar the more prolonged the hyperglycaemia. The most likely explanation is that one cause of sustained hyperglycaemia in these tests is an initial slow absorption of glucose. We were encouraged in the belief that the initial slope indicates rate of absorption of glucose when we found that it was correlated with the time in which iodide appeared in the saliva after ingestion of potassium iodide, in the test of Heath and Fullerton (1935) performed on the same patients. It therefore seems probable, at any rate with a constant daily carbohydrate intake as in this work, that the most important factor determining the shape of the O.G.T. curve in depression is absorption from the alimentary tract.

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Dr. Derek Richter: *Biochemical Aspects of Anxiety (From the Central Pathological Laboratory and Mill Hill Emergency Hospital, London, N.W.7).*—During the last few years there have been a number of useful additions to our knowledge of the biochemical changes produced by emotion. Milhorat and his collaborators (1943) have reported the presence in the blood of patients with anxiety of a substance which has a special action on plain muscle. This substance, which they test for with loops of rabbit intestine suspended in Ringer-Tyrode solution, is not present in the blood of normal controls. Its action on the rabbit intestine is unlike that of adrenaline or acetylcholine, for it produces rhythmic changes in the amplitude of the contraction. The nature of the substance is still unknown, but it presents a promising problem for investigation. Substances which affect plain muscle are of particular interest in connexion with the study of asthma, migraine and other allergic conditions which may be precipitated by anxiety, for the way in which anxiety influences them is still a mystery. It has been suggested that histamine release may play a part here and in this connexion an important advance has been made by Anrep and his collaborators (1944), who have succeeded in obtaining direct evidence of the mechanism by which histamine is inactivated in the body. Previous investigators have generally assumed that histamine was destroyed by the enzyme histaminase, which has been shown to oxidize histamine *in vitro*, but Anrep has shown that histamine administered by mouth or subcutaneously is eliminated in the form of a conjugated derivative together with some free histamine in the urine. The elimination in this way is nearly quantitative. This work suggests that the estimation of the histamine excretion might give useful information in those clinical conditions in which histamine is believed to play a part.

It is well established that anxiety may have a profound effect on the endocrine balance. This is shown, for example, by the endocrine changes in anorexia nervosa and by the effects of anxiety on sexual function. Some interesting new data have been obtained by animal experiments in which emotional strains of anxious rats have been specially bred and their endocrine make-up has been compared with that of normal animals. The tendency to anxiety was judged from the general timidity and non-aggressiveness and from their giving evidence of anxiety by defecating and micturating when introduced into strange surroundings. In addition to a number of minor differences it was found that the thyroid glands were heavier in both sexes in animals of the emotional strain (Yeakel and Rhoades, 1941).

Rennie and Howard (1942) have reported the occurrence of hypoglycæmia as a result of emotional tension in certain individuals and this agrees with the work of Gellhorn. Feldman and Allen (1942), who have demonstrated an increased liberation of insulin into the blood in emotional excitement, a change which is marked in schizophrenic subjects. They estimated the insulin in the blood by injecting it into hypophysectomized and adrenalectomized rats, in which they noted the fall in the blood-sugar level. Although the idea of endocrine changes in emotion is not new, the demonstration of an endocrine change that can be measured in this way in human subjects must be counted as a considerable advance.

The occurrence of hyperglycæmia in anxiety and fear has frequently been reported. Cannon, from his observations on emotional hyperglycæmia in the cat, regarded this as an important physiological mechanism for providing the muscles with sugar as fuel for fight or flight: but Whitehorn (1934), Mann (1925) and McCowan and Quastel (1931), who worked mainly with psychotic subjects, were unable to confirm the view that hyperglycæmia is characteristic of emotional excitement in man. Further information on this point was obtained in some experiments carried out at Mill Hill in collaboration with Dr. Maxwell Jones. At the time when air raids were occurring nightly we collected a group of patients with anxiety states who volunteered to forgo

their evening meal and to leave the shelters during an air raid and come to the top of the building, where samples for blood-sugar estimations were taken. The blood samples were taken at a time when there was gunfire overhead and enemy planes were in the vicinity; most of the patients expressed subjective feelings of fear and gave objective evidence of it. Blood samples for comparison were taken before the raid and after the patient had returned to the shelters. The estimations showed that in 13 out of 18 patients there was no change in the blood-sugar level during the raid. In 5 subjects there was a slight rise in the blood-sugar level, but the highest value was only 115 mg./100 ml., which was hardly outside the normal range. This result was confirmed in a number of other experiments. During the time of the air raids on London I got into the habit of carrying a set of blood-sugar tubes in my breast pocket and testing my own blood-sugar level when there was enemy activity near at hand. Although there were several occurrences which, according to Cannon's views, might have been expected to provoke a hyperglycemia, the blood-sugar never showed more than minor fluctuations of less than 10 mg./100 ml. It was concluded that the blood-sugar response in man varies with the individual: in the majority there is no change, in about a third there is a definite rise in the blood-sugar in emotion, while in a few there may be a hypoglycemic response. The rise in the blood-sugar level, when it occurs, is never as great as might be occasioned by ingesting a few grammes of carbohydrate. It would therefore appear that emotional hyperglycemia is not a mechanism of any great physiological significance in man.

Another blood factor that we have been interested in at Mill Hill is the serum choline esterase. The rise in the activity of this enzyme in anxiety, which was first reported by Tod and Jones (1937), was readily confirmed and further experiments showed that the effect is specific for the choline esterase, since no similar change was found in the serum amylase or in other serum proteins (Richter and Lee, 1942). The problem then arose of the physiological significance of the change. Many attempts to produce the effect artificially by injecting adrenaline, histamine and other drugs were unsuccessful, but it was finally found that the serum choline esterase activity was raised as a result of vigorous muscular exercise (Croft and Richter, 1943). High serum choline esterase activities have been found in patients with acute anxiety states, acute depressive states, post-concussional states and thyrotoxicosis, while the activity has been shown to rise as a result of insulin shock therapy, childbirth and muscular exercise. Low activities, on the other hand, have been observed in stupor, during treatment with narcotics, in states of extreme debility, in advanced senility, in acute infections and particularly in liver disease and in the reticuloses. The evidence suggests that the raised esterase activity found in anxiety may be due to the increased autonomic activity or the neuromuscular activity associated with increased muscular tension. In attempting to differentiate between these two factors it was observed that the esterase activity could be raised by exposure to low temperatures: it would therefore appear that autonomic activity alone can produce a change.

Before leaving the subject of the biochemical effects of anxiety a fascinating account by Wolff (1943) of the circulatory and secretory changes of the gastric mucosa may be mentioned. He was able to observe these changes directly in a patient with a gastric fistula and to study over long periods the effects of different emotional states. In anxiety, hypersecretion and hyperaemia were accompanied by increased motility and increased sensitivity to pain.

Besides these well-established effects of anxiety there are a number of reputed effects which have remained controversial. The occurrence of emotional leucocytosis, which has been reported by a number of investigators, could not be confirmed by Hill and Taylor (1938) in patients with anxiety states. Apparent disagreements of this kind may be due in some cases to differences in the selection of the patients. This was seen very clearly in the course of some work at Mill Hill in which we were collecting patients with acute anxiety states. While most of the patients appeared tense, anxious and self-absorbed when they came to the laboratory to be tested, there were others who showed no signs of overt anxiety. This was so in the case of a young sailor who had been engaging in homosexual practices which he was very much afraid might get found out. He showed marked anxiety when he came into contact with anyone who was in authority, but during the rest of the time he was apparently free from symptoms. It would appear important from a biochemical point of view at least to differentiate between those who are anxious during only a small part of the day and those who remain persistently tense and anxious day and night.

Differences in the selection of subjects may explain some of the divergent results of different investigators, but it must also be remembered that individuals differ considerably in their response to emotion. Cannon and his associates built up a picture of

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the form of sudden anxiety over air raids in individuals who were not normally greatly affected by them.

It would appear that almost any physical inadequacy to which the individual cannot adjust, whether it is due to malnutrition, constitutional inferiority or disease, may give rise to anxiety. Indeed anxiety may be regarded as serving a useful purpose in adapting the behaviour to a physical inadequacy for coping with the demands of the environment. This was seen in many cases of "post-infective effort syndrome" in which general debility interfered with the demands of military training and led to the development of anxiety symptoms. Jones and Scarisbrick (1945) have recently described a type of constitutional impairment of physical efficiency characterized by an abnormal rise in the blood lactate and an abnormally high oxygen requirement in the performance of physical work. Individuals with this condition give a lifelong history of poor effort response. They may be well adjusted in civil life, but under Army conditions their physical disability renders them specially liable to break down and develop anxiety neuroses. This investigation illustrates well the way in which anxiety may be caused by a biochemical lesion.

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Dr. J. H. Quastel [Summary]: The work of Quastel and Wales on hippuric acid excretion in catatonic patients has been largely confirmed by two independent sets of workers but Ström-Olsen, Greville and Lennon have failed to obtain similar results. There was agreement that a small but not insignificant proportion of non-catatonic schizophrenic patients give abnormally low hippuric acid excretion rates. The reasons for the diversity of results obtained in the different hospitals are not easy to discover, but clearly the clinical condition of the patient at the time of the test is an important factor. Diagnosis, also, may vary in a field where there may be many borderline cases, and where difference in opinion between psychiatrists is likely to exist. The best material for the biochemist is a small field, such as that investigated by Gjessing, where there is some approach to homogeneity among the cases. It is essential in work such as this that there must be a high degree of association and co-operation between psychiatrist and biochemist with mutual understanding of the difficulties and points at issue.

With reference to the work on glucose tolerance and emotional states it should be borne in mind that Lockwood, by means of the psychogalvanometer, has confirmed the findings of McCowan and Quastel that a parallelism exists between the hyperglycæmic index and the affective state in manic-depressive disorders.

So far as brain respiration is concerned, although there is as yet no convincing evidence that impaired oxidations in the brain play an important part in schizophrenia, the sensitivity of the cortex to anoxia is such that localized changes may result in abnormal mental manifestations with but little overall change in the brain metabolism. Not only should availability of oxygen or of glucose to the brain tissue be taken into account, but a variety of other factors indispensable for the normal rate of oxygen consumption in the cell must be considered. Among such factors are nicotinamide, aneurine, riboflavin, and adenylypyrophosphate. Local deficiencies of these substances or some interference with their activities may lead to disturbances in the nervous system, as far-reaching in their consequences as deprivation of oxygen or of glucose.

Mention should be made of the interesting results now being obtained with the use of the electro-encephalogram on the connexion between the biochemical activities of the brain and its electro-physiological properties.

Mr. R. Benesch (Maudsley Hospital Research Fellow): The relation of some vitamin deficiencies to certain types of mental disorder has now become generally recognized. Among these the B avitaminoses and especially the nicotinamide deficiency syndromes—i.e. pellagra as well as the acute psychoses of the Cleckley-Sydenstricker type—occupy an

physiological and biochemical changes in anger, fear, rage and pain all mediated by the sympathetic system and designed for the preservation of the individual in fight or flight; but in actual fact it may be questioned whether the responses of different individuals conform to a uniform pattern of this kind. The variability of the blood-sugar response has already been mentioned and this would appear to apply also to the emotional leucocytosis and other biochemical changes. During the air raids it was evident that while some subjects turned 'white' when the bombs came down, there were others who flushed red in the face; while some became tense and hyperactive, there were others who felt faint; in some the discharge was mainly through the sympathetic, but in others through the parasympathetic division. If this variability is true of the physiological responses, it is likely to be equally true of the biochemical. As for Cannon's views on the biological utility of these changes in fight or flight, the evidence here is unconvincing. Jones and Mellersh (1945) have shown that anxiety decreases the ability of the individual to perform muscular feats, since the oxygen uptake and blood lactate rise for a given piece of work are greater than normal in anxious subjects.

Instead of the systematic adaptation of the individual for fight or flight envisaged by Cannon, one finds a series of comparatively variable and unco-ordinated autonomic discharges in which almost any biochemical factor may be involved. Some changes are found more often than others, but there is little evidence of any strictly uniform pattern of responses that one should expect to find in every patient with anxiety. The picture is more like that of a rabbit caught in a trap and throwing itself about blindly in frantic efforts to escape. If anxiety is regarded as a conflict between the individual and his environment, there would appear to be no need to regard the physiological changes in anxiety as attributable to anything more than an increased tonus in those neural regulatory mechanisms (thermal, &c.) by which the individual most commonly adapts himself to changes in his environment; a discharge will then occur through whichever pathways happen to have the lowest threshold values.

The relationship of biochemistry to anxiety is a dual one: anxiety produces numerous biochemical effects, but on the other hand certain biochemical factors can influence the emotional state and may provoke anxiety. Biochemical factors must therefore be considered in connexion with the problem of why some individuals develop anxiety states while others do not, in any particular situation. Hypoglycaemia is among the factors that may induce anxiety and the stimulating work of Hill, Sargant and Heppenstall (1943) and others on the electro-encephalogram is helping to elucidate the mechanism by which the blood-sugar level influences the brain. Anxiety has been reported as one of the earliest symptoms of vitamin B₁₂ deficiency; this was brought out very clearly in the work of Williams and Mason (1941) who observed anxiety, breathlessness, palpitations and fatigue in a series of subjects who volunteered to subsist on a vitamin B₁₂-deficient diet. These symptoms are closely similar to those found in patients with "effort syndrome", but vitamin B₁₂ saturation and excretion tests have shown that avitaminosis is not concerned as an aetiological factor in that condition (Croft, Jones and Richter, 1944).

Recent work has provided some fresh information on the question of whether adrenaline, by itself, can provoke anxiety. Thorley (1942) has confirmed the observation that anxiety is readily provoked in patients with anxiety states by injecting adrenaline; but such experiments have been criticized on the grounds that the anxiety might result from the situation in which the subject is injected with a potent drug rather than from the adrenaline itself. I have recently come across a case of a young aircrewman with an adrenal medullary tumour; the case has been reported in full by Mackeith (1944). The tumour, which was removed by operation, contained over 400 mg. adrenaline, compared with about 7 mg. in a normal adrenal gland. The interest of this patient was that his symptoms started a long time before the tumour was diagnosed: they were brought on by leaning to the left (the tumour was on the left side), by crouching or by muscular effort during drill. He complained of palpitations, nausea, trembling, anxiety and faintness, after which he felt weak. He appeared to be normally well adjusted, but he experienced definite nervousness and anxiety during these attacks. It could hardly be denied that anxiety was produced in this case by adrenaline: but it might be wrong to conclude that this effect is specific for adrenaline. While engaged in clinical work during the last few years in the wards of a general hospital, I have been struck by the frequency with which anxiety may be the first symptom in almost any severe illness. If one asks a patient the first symptom of his illness, he will generally describe some ache or pain, for that is the traditional thing to tell a doctor about; but if one then asks him what he was doing the night before the pain started, or the week before, the onset of anxiety can often be elicited. In many cases this took

in amounts calculated to secure at least the same blood levels as those produced by the "sterilising sulphonamide", had no significant effect (fig. 3). This was interpreted as demonstrating the biosynthesis of nicotinamide by the intestinal flora, the nicotinamide production of which was inhibited by the bacteriostatic effect of the succinylsulphathiazole.

(2) This hypothesis was further tested by studying the nicotinic acid metabolism of the mixed flora, obtained directly from the human cæcum and it was found that considerable synthesis occurs under aerobic conditions, whilst actual destruction of the vitamin takes place anaerobically (Benesch, 1945).

The implication of these findings for the understanding of the pathogenesis of pellagra and similar deficiencies is considerable and can only be very briefly indicated here.

It seems justifiable to conclude that the *nicotinic acid content* of the diet cannot be regarded any longer as the principal factor in the causation of the avitaminoses under discussion, since the body can apparently rely to a large extent on an extradietary source of the vitamin, although admittedly large individual variations do occur in this respect. It must, however, be stressed that the type of diet should more than ever be regarded as being of crucial importance, since the substrate for the vitamin-synthesizing intestinal flora is naturally derived from the ingested food. It is this consideration which permits of a new interpretation of some of the paradoxes connected with the ætiology of pellagra. It is, for example, a remarkable fact, first stressed by Goldberger himself, that milk and eggs are eminently pellagra-preventive foods. The U.S. Public Health Service even puts milk at the head of a list of such foods on the basis of results reported in 1932 by Wheeler and Sebrell. Milk and eggs are, however, to quote Cheldelin and Williams (1942) "extremely poor sources" of nicotinic acid. Maize, on the other hand, contains more nicotinic acid than oats and rye (Barton-Wright, 1944) and not much less than wheat. Yet this cereal is universally associated with a pellagra-producing diet. All these contradictions, which only became apparent when nicotinic acid and certain other of its derivatives were identified as the anti-pellagra vitamin in 1937, could well be understood in the light of the primary effect of such dietary articles on the vitamin synthesizing and destroying activities of the bowel flora. It is well to remember, that Goldberger for a long time regarded pellagra as a protein deficiency and only discarded this view when he found that relatively small quantities of yeast would cure the disease. From what is known about the effect of dietary protein in encouraging the intestinal coliforms (Porter, Weinstein and Rettger, 1938; Mitchell and Isbell, 1942), as well as the selective effect of the "sterilizing" sulphonamides on this section of the bowel flora (Gant, &c., 1943) and the effect of these drugs on nicotinamide metabolism (Ellinger and colleagues, 1944 and 1945), the hypothesis suggests itself that protein by maintaining the right type of flora prevents the development of a nicotinamide deficiency, irrespective of the nicotinic acid content of the protein food fed. This would explain why milk and meat are found to be similarly effective as pellagra-preventive foods, even though they differ so greatly in their nicotinic acid content.

Finally I would like to raise a point which, though problematical, may be of importance in relation to the type of acute psychosis—described by Cleckley, Sydenstricker and Geeslin (1939) in America and by Gottlieb (1944) in this country—which responds so well to nicotinic acid therapy and is therefore rightly or wrongly regarded as a vitamin deficiency. One of the features of this syndrome seems to be that it occurs mostly in elderly people. The discovery of the biosynthesis of nicotinamide led me to suspect a defect in this mechanism as a possible factor in the causation of this syndrome. This could be brought about by the defective diet frequently encountered in such patients, and perhaps by other factors which tend to produce a milieu in the bowel detrimental to nicotinamide synthesis. Some support for this view can be found in the work of Horwood and Nalchajian (1942), who found that in starved and emaciated persons *A. aerogenes* was less common than *E. coli* in the small intestine, whilst in well-nourished persons *A. aerogenes* was the predominating organism. All the persons in this series, which was investigated post-mortem, were over the age of 55. These facts seem rather significant when we consider the results of Burkholder and McVeigh (1942) in the following table:

VITAMIN CONTENT OF BACTERIAL CULTURES GROWN FOR FORTY-EIGHT HOURS AT 360° C.

	Biotin	Riboflavin	Aneurine	Nicotinic acid
<i>Escherichia coli</i>	1.050	0.048	0.075	0.025
<i>Bacterium aerogenes</i>	2.370	0.140	0.148	0.300
	milligramma per ml.	gamma per ml.	gamma per ml.	gamma per ml.

It can be seen that *B. aerogenes* synthesizes considerably greater amounts of aneurine, riboflavin, biotin and especially nicotinic acid than *E. coli*. In the case of nicotinic acid the ratio is as great as 10 : 1.

important place. It is the purpose of this contribution to record some of the findings which have resulted from biochemical investigations on the nicotinamide deficiency syndromes during the last two years at the Central Pathological Laboratory, Maudsley Hospital.

The aim of these studies was twofold: (1) An attempt was made to find a satisfactory biochemical test for the assessment of a person's nicotinamide status and to try and relate these results to the clinical evidence available. (2) The pathogenesis of pellagra and allied deficiency syndromes was studied with a view to removing some of the inconsistencies and even paradoxes associated with the aetiology of these diseases.

In view of the limited time available, I must confine myself to saying that as a result of the finding that nicotinamide methochloride was the main metabolite of nicotinamide in the human body (Huff and Perlzweig, 1943; Ellinger and Coulson, 1943), an eight-day saturation test, based on the elimination of this substance before and after dosage, was adopted as a test for the assessment of the nicotinamide status (fig. 1).

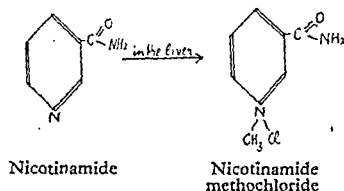


FIG. 1.—The transformation of nicotinamide in the body.

In such experiments—undertaken in collaboration with Dr. P. Ellinger of the Lister Institute—on a series of twelve deficient persons, including acute and chronic pellagrins as well as acute psychotics with a suspected deficiency, it was demonstrated that large differences exist both in the basal output of nicotinamide methochloride and even more clearly in the response to dosage with nicotinamide, between these deficient subjects and a comparable group of controls (fig. 2) (Ellinger, Benesch and Mardivick, 1945).

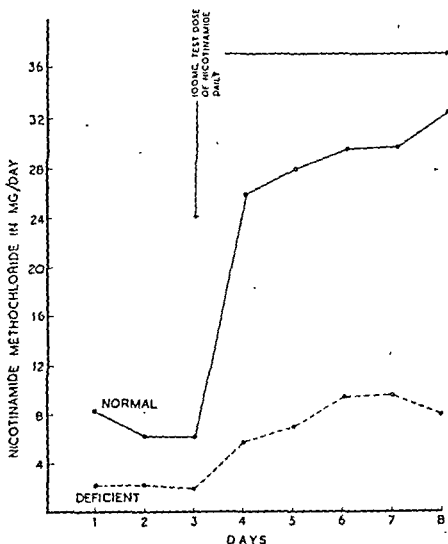


FIG. 2.—Nicotinamide saturation curves of normal and deficient persons.

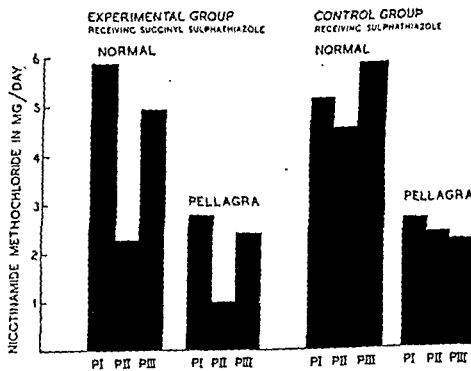


FIG. 3.—Effect of bowel "sterilization" on the nicotinamide metabolism in man.

It is also pertinent to note that the degree of chemical unsaturation, as seen from the tests, agreed on the whole very well with the clinical evidence as to the severity of the syndromes, supplied by the various physicians in charge of the cases.

The other part of the research programme, relating to questions about the pathogenesis of pellagra, centred mainly around the discovery that the human intestinal flora is capable of synthesizing nicotinamide.

This was done in two separate ways: (1) It was shown in collaboration with Dr. Ellinger (Ellinger, Coulson and Benesch, 1944; Ellinger, Benesch and Kay, 1945) that both in normals and pellagrins there was a sharp drop in the daily elimination of nicotinamide methochloride, when succinylsulphathiazole was given and that the level returned to normal when the drug was discontinued. Sulphathiazole used as a control

in amounts calculated to secure at least the same blood levels as those produced by the "sterilising sulphonamide", had no significant effect (fig. 3). This was interpreted as demonstrating the biosynthesis of nicotinamide by the intestinal flora, the nicotinamide production of which was inhibited by the bacteriostatic effect of the succinylsulphathiazole.

(2) This hypothesis was further tested by studying the nicotinic acid metabolism of the mixed flora, obtained directly from the human caecum and it was found that considerable synthesis occurs under aerobic conditions, whilst actual destruction of the vitamin takes place anaerobically (Benesch, 1945).

The implication of these findings for the understanding of the pathogenesis of pellagra and similar deficiencies is considerable and can only be very briefly indicated here.

It seems justifiable to conclude that the nicotinic acid content of the diet cannot be regarded any longer as the principal factor in the causation of the avitaminoses under discussion, since the body can apparently rely to a large extent on an extradietary source of the vitamin, although admittedly large individual variations do occur in this respect. It must, however, be stressed that the type of diet should more than ever be regarded as being of crucial importance, since the substrate for the vitamin-synthesizing intestinal flora is naturally derived from the ingested food. It is this consideration which permits of a new interpretation of some of the paradoxes connected with the aetiology of pellagra. It is, for example, a remarkable fact, first stressed by Goldberger himself, that milk and eggs are eminently pellagra-preventive foods. The U.S. Public Health Service even puts milk at the head of a list of such foods on the basis of results reported in 1932 by Wheeler and Sebrell. Milk and eggs are, however, to quote Cheldelin and Williams (1942) "extremely poor sources" of nicotinic acid. Maize, on the other hand, contains more nicotinic acid than oats and rye (Barton-Wright, 1944) and not much less than wheat. Yet this cereal is universally associated with a pellagra-producing diet. All these contradictions, which only became apparent when nicotinic acid and certain other of its derivatives were identified as the anti-pellagra vitamin in 1937, could well be understood in the light of the primary effect of such dietary articles on the vitamin synthesizing and destroying activities of the bowel flora. It is well to remember, that Goldberger for a long time regarded pellagra as a protein deficiency and only discarded this view when he found that relatively small quantities of yeast would cure the disease. From what is known about the effect of dietary protein in encouraging the intestinal coliforms (Porter, Weinstein and Rettger, 1938; Mitchell and Isbell, 1942), as well as the selective effect of the "sterilizing" sulphonamides on this section of the bowel flora (Gant, &c., 1943) and the effect of these drugs on nicotinamide metabolism (Ellinger and colleagues, 1944 and 1945), the hypothesis suggests itself that protein by maintaining the right type of flora prevents the development of a nicotinamide deficiency, irrespective of the nicotinic acid content of the protein food fed. This would explain why milk and meat are found to be similarly effective as pellagra-preventive foods, even though they differ so greatly in their nicotinic acid content.

Finally I would like to raise a point which, though problematical, may be of importance in relation to the type of acute psychosis—described by Cleckley, Sydenstricker and Geeslin (1939) in America and by Gottlieb (1944) in this country—which responds so well to nicotinic acid therapy and is therefore rightly or wrongly regarded as a vitamin deficiency. One of the features of this syndrome seems to be that it occurs mostly in elderly people. The discovery of the biosynthesis of nicotinamide led me to suspect a defect in this mechanism as a possible factor in the causation of this syndrome. This could be brought about by the defective diet frequently encountered in such patients, and perhaps by other factors which tend to produce a milieu in the bowel detrimental to nicotinamide synthesis. Some support for this view can be found in the work of Horwood and Nalchajian (1942), who found that in starved and emaciated persons *A. aerogenes* was less common than *E. coli* in the small intestine, whilst in well-nourished persons *A. aerogenes* was the predominating organism. All the persons in this series, which was investigated post-mortem, were over the age of 55. These facts seem rather significant when we consider the results of Burkholder and McVeigh (1942) in the following table:

VITAMIN CONTENT OF BACTERIAL CULTURES GROWN FOR FORTY-EIGHT HOURS AT 360° C.

	Biotin	Riboflavin	Aneurine	Nicotinic acid
<i>Escherichia coli</i>	1.050	0.048	0.075	0.028
<i>Bacterium aerogenes</i>	2.370	0.140	0.148	0.300
	milligramma per ml.	gamma per ml.	gamma per ml.	gamma per ml.

It can be seen that *B. aerogenes* synthesizes considerably greater amounts of aneurine, riboflavin, biotin and especially nicotinic acid than *E. coli*. In the case of nicotinic acid the ratio is as great as 10 : 1.

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[June 5, 1945]

PAPERS BY MEMBERS OF THE COMMISSION OF AMERICAN PSYCHIATRISTS

Recent Civilian Experiences with Psychiatric Rehabilitation

By LEO H. BARTEMEIER, M.D.

It has been estimated that about 600,000 veterans of the Armed Forces of the United States have been discharged for psychiatric reasons and this number is being augmented at the rate of approximately one thousand per day. Conceding the fact that perhaps 50% of this number will not need treatment, because their symptoms disappear once they have re-established their family ties and returned to their jobs, and that many more—perhaps another 25%—will not recover so promptly but will not seek or accept treatment, there remains a considerable number, which is certain to be augmented, who need treatment and want it and would take it but are unable to get it. What shall they do? They are not in the Armed Forces any longer so they can expect nothing from the Army. Our Veterans' Bureau should be the natural facility to consider but many of us feel that it is not at all prepared to do the job. There are an insufficient number of out-patient psychiatric clinics and those which do exist are not able to take adequate care of all the civilian patients who seek treatment. Psychiatrists in private practice are also too busy with civilian patients. These were the facts which faced us in the spring of 1944. We were lacking any national leadership for the solution of this problem, but, as is characteristic of our country, various local solutions have sprung up. These have been established through the initiative of groups of psychiatrists in some of our largest cities. While these local efforts are admittedly only partial and incomplete solutions, they serve perhaps to set a pattern which in time may be influential in planning a national programme.

The effort to do something on behalf of the discharged veterans returning to Michigan (Pop. 5,000,000) with psychiatric conditions became the concern of the membership of the Michigan Society of Neurology and Psychiatry in the early spring of 1944 and our War Effort Committee set about to establish psychiatric clinics throughout the State on a regional basis. These clinics have been twelve months in the making and before I left my country in April nine of them were already functioning. Detroit is our largest centre of population and our clinic in that city is naturally the one with which I have been most closely identified.

In planning to set up this clinic we tried to think about the men who would be coming there for treatment and the importance of the clinic being accepted by organized medicine, the various social agencies and the civilian population. No psychiatric clinic for veterans had ever previously existed in our community. Our first step then was to obtain the official approval of our State Medical Society, and perhaps the emergency of the problem with which we were concerned went far toward the immediate and whole-hearted co-operation we received from our medical colleagues who made it possible for us to

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The Central Veterans' Information Bureau, which acts as a clearing station and referral centre for all veterans who need information regarding financial problems, employment and educational opportunities and sources of medical assistance, has turned out to be the largest referral source of patients coming to our clinic, and plans are under way to obtain the services of a psychiatric social worker, as part of the staff of the Veterans' Information Bureau, who would ascertain those veterans needing psychiatric treatment. We also made contacts with the personnel directors of our large industrial corporations and with the administrators of our public educational system. Good working relationships with these groups would facilitate the rehabilitation of veterans under our professional care. We arranged with the various social agencies in our community to abstract the historical material on those cases which they wished to refer to us so that we could know in advance whether or not the patients they wished to send us were ones with whom we should attempt psychotherapy.

Eighteen Detroit psychiatrists volunteered their professional services without remuneration and are giving approximately two hours of their time each week. Patients are seen three evenings a week and the Clinic may soon be open on four evenings each week. An experienced psychiatric social worker, who acts as executive assistant during the day, together with a clinic secretary and a receptionist constitute the full-time staff, and plans are under way to acquire an additional psychiatric social worker. The clinic began receiving patients February 6 of this year and 106 veterans had been given psychiatric assistance by April 20. Patients are seen by appointment and treated very much the same as patients who consult psychiatrists in private practice. Each patient usually spends approximately one hour with the psychiatrist at the time of his first visit and the time allowed for the subsequent interviews is determined by the individual therapist.

Our clinic has been established with three principal objectives: the first and most important of these is the adequate treatment of these psychiatric casualties of war; the second is the maintenance of suitable medical records for the purpose of clinical research; the third is the teaching of the psychiatrists who work in the clinic through regular monthly staff conferences during which therapeutic techniques, &c., are discussed in detail. It may be of interest to note parenthetically that these psychiatrists have worked diligently and with enthusiasm and there is every reason to believe that the work of this clinic will ultimately become an important facet of the life of the community.

The Value of Induced Dissociated States in the Therapeutic Process

By LAWRENCE S. KUBIE, M.D.

I wish to report the tentative conclusions which have grown out of recent experiments with modifications of analytic techniques. These modifications were designed both to shorten the therapeutic process, and to overcome some of the obstacles to success which psychoanalysis often encounters. All of these experiments involved the induction of controlled states of partial dissociation [4, 5, 6, 7, 8].

Originality cannot be claimed for this work, beyond certain technical innovations and syntheses. Many workers in England have been pioneers in exploring this field, notably Hadfield [2] and Horsley [3], and in America, Grinker and Spiegel [1] and others. Our own work is an extension of theirs, with the application of certain basic physiological and analytical principles.

It will be our thesis that in human psychological processes there is a continuous interplay between two opposing tendencies. On the one hand, whenever we repress unacceptable ideas, feelings and impulses, we dissociate from the repressed processes their attached energies. On the other hand at the same time there is an equally continuous unconscious effort to lift these repressions and to reintegrate the dissociated energies. Every psychotherapeutic procedure must be understood in terms of its influence on the dynamics of this unstable equilibrium. Repression, dissociation, reintegration, and recall are thus seen to be four aspects of a single complex psychological process.

It is always somewhat dangerous to dissect a complex constellation into logical partitions, attaching special names to its various aspects; because this leads to the logical error of treating different words as though each was a separate dynamic entity with independent laws and energies. Thus we tend to speak of repression and dissociation as though they were separate mental mechanisms: yet repression cannot occur without

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dissociation, or vice versa. Nor can either of these exist apart from reintegration and recall. No one of these has an energetic system of its own. Analytic terminology and analytic theory have suffered much from such misapplication of these concepts. If then I single out for emphasis that aspect which we call dissociation, this is largely because it seems necessary to shift our attention from the integrative aspects of the process. Integration is of course the most obvious goal of psychotherapy; but it is hardly helpful or enlightening to talk of a goal as if it were a technique of therapy: as though "health" were a medicine by which to get well. We cannot "integrate" anyone: we can only remove obstacles to integration. It is in this sense that induced states of partial dissociation can be used to release spontaneous reintegrative processes in the struggle for therapy.

While dissociative tendencies are inseparable from all mental phenomena, the induced state of partial dissociation is seen most characteristically in normal sleep, and in all way-stations on the path to sleep, such as the spontaneous hypnagogic reverie, or the induced hypnotic trance. It is as much a part of these states as it is of the more dramatic phenomena, such as multiple personality, to which the concept of dissociation is often erroneously restricted.

How then can induced states of partial dissociation be harnessed to the therapeutic or re-integrative process? This is the question which I will attempt to answer. In the brief time at my disposal, however, I will not be able to present either experimental evidence or clinical illustrations. I will be able only to make clear the hypothesis which has grown out of our experiments and observations.

Various degrees of dissociation were produced by monotonous physiological stimuli, both with and without a wide variety of drugs. These manoeuvres induced a condition which lies somewhere between sleeping and waking, in which the individual views himself and his life with some measure of detachment, much as a dreamer may observe himself in action in a dream. This state is further marked by a tendency to return automatically to important storm centres of emotional turmoil. In this respect also the process resembles the dream but without the condensations and distortions of the dream, and with more spontaneous activity and an automatic, somnambulistic discharge of emotions through appropriate behaviour. Among the drugs used were the volatile anaesthetics (such as ether and nitrous-oxide-oxygen), the barbiturates, combinations of hyoscine and other drugs, derivatives of cannabis indica, alcohol, hypoglycæmic conditions induced by insulin, and even the twilight states that may follow shock therapy. No specificity could be observed in any of these drugs, nor in any one procedure; but sedative drugs were of special value in the induction of the degree of dissociation described, by lessening the individual's hold on reality and by lessening the intensity of his emotional alarms.

It is remarkable to observe how in such partially dissociated states the thoughts and feelings of the patient revert spontaneously to his troubles. It has been suggested (Kubie and Margolin [8]) that "this is because such storm centres have a higher threshold for narcosis than do less highly charged areas, just as anoxia can bring to light clinical manifestations of sub-clinical focal brain drainage". Perhaps as a consequence of this, mild narcosis can inhibit non-conflictual areas and leave the emotionally charged areas to stand out in high relief. This in turn leads to a more direct recovery of memories of early traumatic experiences than is possible even with the most painstaking use of free associations in the fully integrated state.

Again it became clear that the action of drugs was never dependent solely upon their chemistry, or the dosage used, or on individual pharmacological idiosyncrasies. On different occasions the same individual would react to identical doses in widely different ways, depending upon the intra-psychoic tensions at work on each occasion.

In the course of our work we learned furthermore that just so long as the dissociated state does not become too complete (if, for instance, a drug is not given in doses large enough to produce profound narcosis) a dynamic relationship with the therapist is continuously maintained. This proved to be a matter of critical importance, because the nature of this relationship between the physician and the narcotized and dissociated patient determined the use to which the material produced by the patient could be put, and the therapeutic integration of that material. In dissociated states the patient often indicates with little or no disguise his multivalent affective attitudes towards the therapist. In so doing he may even show clearly the sources of the displaced emotional attitudes which he has transferred from earlier years, often mis-identifying the therapist with his parents or other important figures. Thus transference attitudes, the sources of which are completely masked in fully conscious states, frequently become transparently clear when a patient is in the dissociated condition. Control of this situation is maintained by constant attention to and manipulation of the transference relationship, precisely as this relationship must be managed in orthodox analytic procedures. The difference

is merely that the transference relationship in states of partial dissociation is frequently more highly charged, more vivid, and more transparent than it is in therapeutic procedures in which the patient is fully conscious and on guard against revealing the inner nature of his attitudes to the therapist.

We also came to realize that the dissociative state is not without its dangers. It is a deliriod reaction in which forces of considerable violence may be released, unleashing at times latent depressions, elations, or paranoid schizophrenic states, which may persist for some time afterwards. This is not a frequent phenomenon; but it is a danger that must be borne in mind, and makes it essential that such work be carried on by men who have had experience in working with powerful unconscious forces.

Similar considerations led us to question the advisability of using prolonged deep narcosis, because of the difficulty of controlling the depth of the narcosis and the severity of the deliriod reaction. Short-acting drugs are safer because the depth of narcosis can be readily controlled and quickly interrupted.

In summary we may say that in the dissociated state the use of free associations, the reliving of the recaptured past, and the manipulation of the transference, together comprise a logical extension of psychoanalytic procedure. In the dissociated state these steps lead directly to repressed material which is at the root of resistances. This often makes it possible to circumvent such resistances. Similarly the phenomena of transference become more transparent and more malleable; and in this state the patient himself seems to be less vulnerable to the exposure of his own highly charged material.

Thus a therapist who is dynamically oriented, and who is thoroughly experienced in dealing with unconscious forces, can both accelerate and control the therapeutic process by balancing the adaptive capacity of the patient to the disturbing quality of the material.

These are some of the conclusions which have led us to hope that in this direction a material shortening and strengthening of the therapeutic process may ultimately be achieved.

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Dr. John Romano (Professor of Psychiatry, University of Cincinnati) read a paper on "Studies of Syncope: Differentiation Between Vasodepressor and Hysterical Fainting". This paper was an abstract of a report presented by Dr. Romano and Dr. George L. Engel at the Annual Meeting of the American Society for Research in Psychosomatic Problems, Chicago, on June 11, 1944. It was published in *Psychosomatic Medicine*, 1945, 7, No. 1.

Constructive Factors in the Personality

By Dr. JOHN C. WHITEHORN¹

THE intensely practical testing of our psychiatric foundations, such as occurs in military experience, gives useful pointers toward the fields of great need in our psychiatric knowledge. The harsh testing of men through prolonged combat experience, and the thoughtful survey of that accumulated experience, emphasize the complexity of considerations which determine stability and durability. Seen from the military viewpoint, the positive forces which hold men together, individually and in fighting units, become psychiatric issues of crucial importance.

I wish to speak of two lines of recent and current investigation in the Phipps Clinic concerned with the satisfactions which people gain out of their relationships to each other, counterbalancing the pains and frustrations inseparable from the business of living as a social organism.

¹ Scientific Consultant and member special mission on study of combat exhaustion, E.T.O., U.S.A.; Henry Phipps Professor of Psychiatry, Johns Hopkins University and Hospital, Baltimore, Maryland, U.S.A.

dissociation, or vice versa. Nor can either of these exist apart from reintegration and recall. No one of these has an energetic system of its own. Analytic terminology and analytic theory have suffered much from such misapplication of these concepts. If then I single out for emphasis that aspect which we call dissociation, this is largely because it seems necessary to shift our attention from the integrative aspects of the process. Integration is of course the most obvious goal of psychotherapy; but it is hardly helpful or enlightening to talk of a goal as if it were a technique of therapy: as though "health" were a medicine by which to get well. We cannot "integrate" anyone; we can only remove obstacles to integration. It is in this sense that induced states of partial dissociation can be used to release spontaneous reintegrative processes in the struggle for therapy.

While dissociative tendencies are inseparable from all mental phenomena, the induced state of partial dissociation is seen most characteristically in normal sleep, and in all way-stations on the path to sleep, such as the spontaneous hypnagogic reverie, or the induced hypnotic trance. It is as much a part of these states as it is of the more dramatic phenomena, such as multiple personality, to which the concept of dissociation is often erroneously restricted.

How then can induced states of partial dissociation be harnessed to the therapeutic or reintegrative process? This is the question which I will attempt to answer. In the brief time at my disposal, however, I will not be able to present either experimental evidence or clinical illustrations. I will be able only to make clear the hypothesis which has grown out of our experiments and observations.

Various degrees of dissociation were produced by monotonous physiological stimuli, both with and without a wide variety of drugs. These manoeuvres induced a condition which lies somewhere between sleeping and waking, in which the individual views himself and his life with some measure of detachment, much as a dreamer may observe himself in action in a dream. This state is further marked by a tendency to return automatically to important storm centres of emotional turmoil. In this respect also the process resembles the dream but without the condensations and distortions of the dream, and with more spontaneous activity and an automatic, somnambulistic discharge of emotions through appropriate behaviour. Among the drugs used were the volatile anaesthetics (such as ether and nitrous-oxide-oxygen), the barbiturates, combinations of hyoscine and other drugs, derivatives of cannabis indica, alcohol, hypoglycemic conditions induced by insulin, and even the twilight states that may follow shock therapy. No specificity could be observed in any of these drugs, nor in any one procedure; but sedative drugs were of special value in the induction of the degree of dissociation described, by lessening the individual's hold on reality and by lessening the intensity of his emotional alarms.

It is remarkable to observe how in such partially dissociated states the thoughts and feelings of the patient revert spontaneously to his troubles. It has been suggested (Kubie and Margolin [8]) that "this is because such storm centres have a higher threshold for narcosis than do less highly charged areas, just as anoxia can bring to light clinical manifestations of sub-clinical focal brain drainage". Perhaps as a consequence of this, mild narcosis can inhibit non-conflictual areas and leave the emotionally charged areas to stand out in high relief. This in turn leads to a more direct recovery of memories of early traumatic experiences than is possible even with the most painstaking use of free associations in the fully integrated state.

Again it became clear that the action of drugs was never dependent solely upon their chemistry, or the dosage used, or on individual pharmacological idiosyncrasies. On different occasions the same individual would react to identical doses in widely different ways, depending upon the intra-psychoic tensions at work on each occasion.

In the course of our work we learned furthermore that just so long as the dissociated state does not become too complete (if, for instance, a drug is not given in doses large enough to produce profound narcosis) a dynamic relationship with the therapist is continuously maintained. This proved to be a matter of critical importance, because the nature of this relationship between the physician and the narcotized and dissociated patient determined the use to which the material produced by the patient could be put, and the therapeutic integration of that material. In dissociated states the patient often indicates with little or no disguise his multivalent affective attitudes towards the therapist. In so doing he may even show clearly the sources of the displaced emotional attitudes which he has transferred from earlier years, often mis-identifying the therapist with his parents or other important figures. Thus transference attitudes, the sources of which are completely masked in fully conscious states, frequently become transparently clear when a patient is in the dissociated condition. Control of this situation is maintained by constant attention to and manipulation of the transference relationship, precisely as this relationship must be managed in orthodox analytic procedures. The difference

Section of Orthopædics

President—ERIC I. LLOYD, F.R.C.S.

[June 23, 1945]

Late Results of Albee Fixation of Tuberculosis of the Spine

By D. McCRAE AITKEN, F.R.C.S.

DURING the past 40 years treatment of tuberculous osteo-arthritis might be said to have passed through two phases and entered on a third. The first phase was the treatment taught by Owen Thomas, namely, fixation of the affected joints on a controlling splint until all pain and all swelling had disappeared and the patient's condition was thriving.

The second stage was ambulatory, with the affected joint still protected in some sort of ambulatory splint. Thomas was slow to operate, but in hospitals such operations as excision of the knee-joint were frequent in the more severe cases. Success depended on very prolonged protection. The second phase may be said to have begun about 1911—first applied in Robert Jones' practice, mainly to tuberculous disease of the spine. This consisted in adding a bone graft with the object of securing extra-articular fixation and bridging the diseased area so securing more complete fixation, but the original principles were always adhered to. The cases treated by the pure Thomas treatment before bone-graft surgery was introduced, were liable to relapse with increasing weight and increasing work, but bone-graft cases have been remarkably free from this defect.

The third or present phase is based on the extraordinary results which follow the successful employment of the Robertson Laval technique which is briefly outlined below. In acute cases of hip, knee or spinal disease, when the focus in the bone can be discovered early and the bone is drilled, a change is produced in the patient's health within a week or ten days, temperature drops and thereafter swings only about a degree in the twenty-four hours, appetite returns, pain disappears. Also in the speaker's practice no departure is made from the old rule of complete fixation until everything is quiet. The results are still too confusing to give any definite rule as to when this method should be employed.

In the case of children treated in an open-air hospital with a hospital school, there is no hurry. Prolonged rest and fixation to correct existing kyphos as much as possible is the most important point, but the question of Albee operation at the age of 13 or 14 years is always borne in mind although successful operations can be performed at a much earlier age. A successful operation depends first on waiting patiently until compensatory changes have taken place and the back looks straight when the patient is turned on the face. It is then possible to put in a graft so as to bridge the diseased area and relieve strain on the bodies of the vertebrae.

After the operation at least three months are allowed to elapse before changing from a Thomas double frame to a Thomas back support. The Thomas back support is preferable to any kind of jacket because it in no way impedes the movement of the ribs and does not interfere with respiration. At the end of three or four months the patient is gradually allowed to get up and walk.

In children the back support is used during the period of growth, perhaps until they are 16 or 17 years old.

It is in adults, however, that the advantages of this operation are most evident. Tuberculous caries of the vertebrae is often missed in the early stages by physicians. Pain in the back without visible deformity is too often called muscle strain or rheumatism and subjected to massage or other palliative treatment, until some sudden jar causes a collapse of the vertebral body and a visible kyphos. All cases of backache should be X-rayed, especially from the lateral view, to see if there is any focus or bone change in the vertebrae. These foci are unmistakable; when visible they are almost invariably rounded blobs in the first stage without any encapsulation.

With prompt recumbent treatment on the Thomas frame, this kyphos frequently disappears but usually from nine to eighteen months should elapse before bone grafting is performed.

Three or four months after the operation the patient gets his short back support and leaves the hospital soon after he is able to walk comfortably. Usually he is allowed to return to light work within twelve months. This is an important economic factor for adults because improvement in the condition of the bodies of the vertebrae may continue for a long time after the patient has got up, and bone graft plus back support make the patient's condition safe from sudden strains.

Persons differ markedly in regard to their capacities for satisfaction in personal contacts and relationships. Dr. Barbara Betz, of our Phipps staff, has been making a psychotherapeutic investigation of a group of patients who could be characterized as obsessive-schizoid. These patients have shown in general minimal capacities for gaining satisfaction in personal relationships and have tended to shrink back into ritualistic or meticulously exact and impersonal performances for their satisfactions. One of the most clear-cut observations by Dr. Betz in this group has been their tendency to specify and limit sharply the role assigned to the physician as the foundation of treatment. Dr. Betz has found it necessary, and often, in the end, helpful, to acquiesce without special struggle, in a rather arbitrarily limited formulation of her functions, expressed or implied. For example, one of these patients was a young man who came for help in a very specific way. He had arrived, intellectually and emotionally, at an attitude of great hostility against the established social order. He had found, however, that he sometimes lost self-control, and had got himself into unexpected quarrels and had made violent attacks. He asked for psychiatric help in gaining a better control and management of this antagonism to the social order, stating very specifically that he would not tolerate any efforts to modify his fundamental antagonism. He just wanted help in keeping out of trouble in the manner of expression of this antagonism. Incidentally, a clue to certain trends in him may be gained from the information that his ambition was to be a maker of surgical instruments.

In the treatment of such patients, the physician may have to wait a long time before the patient can tolerate any reactions on the doctor's part which go beyond the limits obsessively set, but there does come a time, fortunately, when sufficient faith and personal trust permit the doctor effectively to challenge the patient, so to speak, in a manner which may elicit less obsessively stereotyped expressions of feeling or attitude. The patient may be said then to have gained courage to react to the doctor like a human being, and to expect from the physician personal consideration and respect when he does so. This point in therapy has been found crucial in determining possibilities of clinical improvement. We have come to think that such patients had been hindered in their personality development previously by a great distrust of themselves as persons, self-warming depersonalization of their conduct, and a resultant failure to elicit the heart-warming reactions from others which are needed for one's encouragement, self-confidence and further emotional growth.

You will gather, I trust, from this rather casual comment upon the studies of these obsessive-schizoid persons, that we have been concerned to study in them the operation of some of the positive and constructive forces in the personality in a manner somewhat comparable to the study of certain gases in partial *vacuo*. The significance of certain factors may not be obvious until studied in such small concentration that it becomes a limiting factor. The small measure of emotional gratifications obtainable from interpersonal relationships seems to constitute, in these individuals, such a limiting factor, until conditions more favourable to its growth have been established, but we consider that such studies of limiting values serve also to direct attention to the importance of interpersonal bonds in maintaining functional integrity in the very trying conditions of combat.

Another investigation at the Phipps Clinic is concerned with a condition of early childhood recently designated by Dr. Leo Kanner as "early infantile autism"—a condition characterized by an extraordinary lack of personal relationship. These are very sick children, practically schizophrenic in behaviour, who have not infrequently been erroneously labelled feeble-minded. We have devoted one of the wards, West 2, to the care of a group of these children, selected by Dr. Kanner, and we plan to study the possibilities of cultivating their personal relationship to certain carefully chosen nursing personnel, and to the physicians. One of the possible explanations of this curious illness may lie in some innate limitation of emotional capacities. It is our intention to test out, as well as we can, the possibilities of stimulating and encouraging whatever potentialities we can discover in these youngsters for more gratifying personal relationships.

I have mentioned these two studies to indicate our interest not only in studying noxious influences and traumatic events, as important factors in psychiatry, but also in recognizing and evaluating the constructive influences which make for good performance and satisfaction, and which therefore have great psychiatric importance in maintaining personal integration under very adverse conditions.

Dr. Karl Menninger read a paper entitled "The trend in psychological education".

Section of Orthopædics

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It is quite usual for these patients to be able to touch their toes with the back support on within a year of getting up. Then they are allowed to leave the back support off on Sundays when they are not working and gradually more often until they no longer need it; X-rays are taken periodically to check up on the condition of the bodies of the vertebrae. The object of performing this operation is to guard the patient against risks of sudden development of a kyphos in muscle strain.

The speaker then demonstrated 7 adult cases showing the result of Albee fixation of the spine by bone graft in tuberculous disease of the bodies of the vertebrae. One was a girl of 20 years of age on whom an Albee fixation had been done on account of a crush fracture in which a detached wedge of bone had failed to re-unite again with the body from which it was broken. Experience has shown that unless the back is fixed these cases are liable to backache and a development of kyphos at a later date, hence the advisability of grafting. The case demonstrated how comfortable these patients are on a Thomas frame although she had been operated upon only four days previously. The other cases had all been going about their normal life for some time, and had all been operated upon five years ago or more. There was only one who could not touch her toes with the knees straight, but she could not do so even as a girl.

Finally, at the present day in addition to the question of extra-articular fixations, there is the question of dealing with the tuberculous disease itself by increasing the resistance of the patient by the Lavallo procedure. The Lavallo procedure is not an operation of orthopaedics, it does nothing to prevent the occurrence of deformity but it is frequently followed by a marked improvement in the well-being of the patient.

The Lavallo procedure is based on inferences drawn from two accepted facts concerning tubercles. The first is the Koch phenomenon (1882) which is that if an animal receive an injection of tubercle bacilli a tubercle is formed at the site of injection and the animal becomes "sensitive" to tuberculin. If an animal so sensitized be given a second injection of tubercle bacilli a local inflammatory reaction occurs at the site of the second inoculation, the regional lymph glands, however, being unaffected. At the same time focal reactions occur in the body, both in the region of the primary nodule, and in any other locality where the bacilli may happen to have lodged. These phenomena are accompanied by severe constitutional disturbance, which, if the second dose of tubercle be very large, may prove fatal.

Professor Lavallo, at that time surgical pathologist, had to report on material from cases of excision of the knee for tuberculous disease; he noted that the cancellous bone tissue was often riddled with tuberculous foci. These were not all of the same age. Some were old and had undergone caseous degeneration, others again showed signs of capsulation but no caseation. Still younger foci were merely dark spots about 0.5 cm. in diameter. Could one of these be a recently formed tubercle, and if so, did it contain some powerfully defensive substance?

On microscopic examination these early foci were found to contain tubercle bacilli (granular type) and the whole primitive granuloma was surrounded by a greyish capsule suggestive of a primitive stage of a fibrous capsule. This tough capsule constricted small veins and lymphatic vessels leading from the part. X-ray examination showed faint blurred spots without any sclerosis of surrounding bone.

The inference was that these faint blurred areas shown in X-rays of living patients were fresh reinfections from older foci and might contain some defensive substance, which could not escape into the general circulation on account of the constriction of issuing capillaries by the tough capsule.

The Lavallo procedure is to bore into the least distinct of such areas from some point in the diaphysis outside the capsule of the joint so as to let the mysterious substance out to the systemic circulation.

Professor Lavallo operated on two cases in this hospital in 1929. The first was a small boy who had been under observation for two years with an acutely painful hip; X-rays during this period showed an increasing degeneration of the head of the femur and acetabulum without any attempt at sclerosis round the foci. Temperature ran from 98° to 101°, loss of weight was progressive and a fatal result was feared. Within a week of the operation the temperature settled to a daily swing of only one degree and the child was out of danger.

Gradually the procedure was adopted in cases that were not doing well. The difficulty was to recognize the very early foci in the X-ray. In many cases operated on the foci chosen were already becoming encapsulated, and in these subsequent revision showed little result. After five years, a year was spent in revising X-rays and following up the cases. The result was encouraging. To-day the first question with a new case of suspected tuberculous joint is whether a sufficiently young focus can be recognized instead of leaving the operation to be used as a last resort.

The subject calls for investigation by a team of clinical observers, surgeons, pathologists and physicians working together. We should know more of the radicles in the tuberculins, those that produce proliferation of the endothelium and round-celled proliferation round them, those that produce the waxy coat which stains by the Ziehl-Neelsen method. Especially important are the granular forms discovered by Much (1908). Much was supported by Fontes (1910-1916).

These forms only are to be found in many cases of low-grade joint lesions, with a subnormal swing of temperature of 2° or more. Are the acute, subacute and chronic forms of joint disease due to different varieties of the bacillus, or to different degrees of natural resistance? Is the young focus in bone comparable with the Ghon tubercle or Parrot's node? In some very acute cases of tuberculous disease in various regions, e.g. hip, knee, vertebrae, there has also been otorrhoea, with perforations of the tympanum

diagnosed as typically tuberculous by an E.N.T. consultant, and the otorrhoea has ceased within three or four weeks after operation on the remote lesion in bone.

The speaker is convinced of the value of this treatment for tuberculosis. The results may be startling but there must be a follow-up for relapse may occur. An operation successful in the first instance may be followed some years later by a fatal nephritis or sudden meningitis. This suggests the need for more careful study of the kidneys at an early stage of the disease before renal symptoms are noted.

Cases of Chronic Suppurative Osteomyelitis.—J. G. O'CONNELL, F.R.C.S.Ed. (for E. P. BROCKMAN, F.R.C.S.).

The prognosis in chronic suppurative osteomyelitis from the point of view of obtaining a complete cure is not good, and it is less good where the femur is the affected bone than in osteomyelitis of any other long bone. This fact has, in the past, led many surgeons to the conclusion that an appreciable percentage of cases of osteomyelitis of the lower end of the femur are better off with an amputation. It is submitted that a limb which remains free of trouble for periods of more than five years, even though there may be an occasional flare-up subsequently and may even ultimately lead to amputation, is in a young adult preferable to an artificial limb.

We have been able to trace 13 cases of osteomyelitis of the femur treated in this hospital over five years ago. Of these 7 have remained completely healed during this period (2 for as long as nine years), 5 have had intermittent minor recurrences, never necessitating prolonged stay in hospital, and 1 has a chronic discharging sinus but is gainfully employed and is not wishful of further interference.

That the treatment of this condition demands patience from both surgeon and patient is shown by the fact that the average stay in this hospital was twenty-three months. However, this figure slightly over-emphasizes the chronicity as in pre-war days children were kept in as long as there was any question of a further breakdown, especially where the home conditions were not satisfactory. In the exigencies of war this policy has had to be modified, but the principle still holds. The following cases of osteomyelitis of the femur were demonstrated:

CASE I.—F., aged 17. In hospital twelve months, two sequestrectomies. This patient is as yet only a three-year cure but the radiographic picture is so good that it is unlikely she will have much further trouble. Her scar is non-adherent and she is symptom-free.

CASE II.—M., aged 14. Treated seven years ago, one minor flare-up which quickly settled down. X-ray shows sclerosis but little evidence of cavitation. Period in hospital twenty-one months—two sequestrectomies.

CASE III.—F., aged 21. Five-year cure. Twenty-seven months in hospital, three operations: two sequestrectomies, one saucerization. X-ray appearances very good. General condition good.

CASE IV.—M., aged 14. Fourteen months in hospital—three sequestrectomies. One slight flare-up as an out-patient—otherwise no trouble for four years.

CASE V.—M., aged 11. Ten months in hospital—one sequestrectomy. Eight years free of symptoms.

CASE VI.—M., aged 12. Ten months in hospital—one sequestrectomy. Eight years free of symptoms.

There are three main principles applied to the treatment of this condition in this hospital:

(1) *Open air and general hygiene treatment.*—It is just as essential that a case of osteomyelitis should be treated in the open air as tubercle. The general condition of the patient has a definite influence on the prognosis of the local condition and the patient must be treated, not just the bone.

(2) *Adequate splintage at all stages.*—This is another factor which is not sufficiently appreciated, particularly in general hospitals. It is just as essential to immobilize osteomyelitis as it is tubercle. For femurs we use a Thomas knee splint with fixed traction except where the upper end or hip-joint is affected when the patient is treated on a Jones abduction frame. After the wounds have healed the patient is allowed up in a weight-bearing caliper which he wears for a varying period.

(3) *Adequate operation at the optimum time.*—The average number of operations performed on osteomyelitis of the femur was four. These included: (a) Simple drainage of soft tissue abscesses; (b) drilling of bone; (c) sequestrectomies and curettings of sinuses; (d) saucerizations; (e) excisions of scar. In every case there is a minimum amount of operative interference until the patient's general condition is good and the local condition is thoroughly cleaned up. Then when the time is ripe, the cavity or cavities in the bone are laid widely open. The overlying soft tissue is freed from scar tissue and the wound is lightly packed with non-adhesive gauze.

Even with the aid of penicillin, cancellous bone grafting and skin grafting these three cardinal principles must be followed.

The newer methods are complementary to the older one. An illustrative case is that of a soldier—wounded in the upper thigh by a machine-gun bullet. In all he was in hospital twenty-three months. He had six operations before admission and seven operations here. At one operation some sequestra were removed but although at subsequent explorations no sequestra were found, profuse discharge from all four sinuses continued.

The diagnosis of osteomyelitis was queried on both clinical and radiological grounds. Ewing's tumour and tuberculosis were both suggested but repeated pathological examination of pus and granulation tissue revealed first pseudo-hemolytic streptococcus and pyocyanus and subsequently *Staph. aureus* and *B. proteus*. The granulation tissue showed chronic inflammatory reaction, no evidence of tuberculosis. A section of the bone showed no evidence of Ewing's tumour.

Finally we succeeded in obtaining some penicillin and he was given a systemic course of 100,000 units daily for three days prior and four days subsequent to operation. At operation all the sinuses were opened up, tubes inserted and 10,000 units instilled. He was given 1,000 units by local instillation subsequent to operation at 3 hourly intervals for seven days. Five weeks later all the wounds were completely healed and have continued so.

Conservative Treatment of Volkmann's Ischæmic Contracture

By J. G. O'CONNELL, F.R.C.S.(Ed.)

THE observation that the flexion contracture of the fingers is diminished on palmar flexion of the wrist has been the basis of the various conservative methods of treatment employed in this condition. These have met with varying degrees of success, but the principle of gradual stretching of the contracted tissues would appear to have more foundation in theory than the various operative measures suggested, such as muscle slides, arthrodesis of wrist, &c.

It must be admitted, however, that in an appreciable percentage of cases conservative treatment alone is inadequate and it becomes necessary to resort to operation. The operation most in favour would appear to be fixation of the wrist in the optimum position.

The first case treated by the method to be described was originally admitted to hospital with a view to performing an arthrodesis of wrist. It was felt that with so severe a degree of contraction present, circulatory obstruction would almost certainly follow sudden correction of the deformity. To ensure against this it was decided that a preliminary course of gradual splintage should be applied to obtain the maximum correction prior to operation. A full-length plaster-of-Paris was applied from below the elbow to beyond the finger-tips with the wrist palmar flexed and the fingers straight. The back of the plaster was cut away to expose the distal interphalangeal joints. The patient was instructed to extend her fingers voluntarily at those joints. A close watch was kept for symptoms of pain or circulatory changes in the finger tips. A stockinet glove and a strip of plaster wool down the flexor aspect of the forearm and wrist were used as padding. This plaster was removed two weeks later when it was found that the patient could actively extend her wrist a further 10 degrees with fingers extended. A new plaster was applied in the position of maximum correction and this plaster remained on for three weeks. Two further changes of plaster were necessary before this wrist came into dorsiflexion with the fingers extended. The wrist and fingers having extended so well it was felt that an arthrodesis may be avoidable so it was decided to persevere with splintage.

It was then found that the hyperextension deformity at the metacarpo-phalangeal joints still persisted and, if the full length plasters were persevered with, appeared likely to be aggravated. Therefore an anterior plaster slab to hold the wrist in 15 degrees of dorsiflexion was applied and individual splints for each finger, after the manner originally described by Robert Jones, were made from two-inch Cellon plaster bandages. The patient was encouraged to flex and extend actively at the metacarpo-phalangeal joints and to report any tendency to flexion. These individual splints and "cock-up" were renewed on two subsequent occasions, and after two months the finger splints were discarded, the "cock-up" splint being retained. The patient was instructed to flex and extend her fingers actively and passively. The "cock-up" was retained for a further three months and then removed. The patient has been under periodical supervision since then and shows no tendency to relapse.

The three cases shown are of Volkmann's Contracture following fractures around the elbow-joint—one of a radius and ulna, the other two being supracondylar fractures of the humerus.

CASE I.—F., aged 9 years.

12.8.43: Supracondylar fracture left humerus.

29.3.44: First seen; well-developed Volkmann's contracture.

27.4.44: Splintage commenced with view to arthrodesis.

7.12.44: Splints discarded.

Result: Very good function. Grip almost as strong as on right. Seen since and has no tendency to relapse.

CASE II.—F., aged 8 years.

25.7.43: Fracture upper third right radius and ulna. Subsequently developed a contracture and was treated as an out-patient at hospital by massage and passive stretching.

11.5.44: First seen at Out-Patient Clinic: Rt. Volkmann's contracture: well developed but not as severe as Case I.

17.5.44: Splintage commenced.

29.11.44: Splints discarded.

Result: Good function, grip almost equal to other side. Cosmetically not as good a result as Case I, but function equal. Is being watched and has shown no tendency to relapse.

CASE III.—M., aged 11 years.

6.9.44: Supracondylar fracture Rt. humerus. Subsequently developed a contracture and was treated by "cock-up" splint and passive stretching.

4.1.45: First seen at Out-Patient Clinic—Volkmann's contracture Rt. forearm. Has a fair range of dorsiflexion at wrist but on dorsiflexion wrist goes into extreme ulnar deviation.

10.1.45: Splintage commenced.

23.5.45: Splints removed.

Result: Good function and has a useful grip. The ulnar deviation proved difficult to correct completely, and rather detracts from the cosmetic result. Has been seen since and shows no tendency to relapse.

It will be noticed that the three cases described are all children. The method has not been tried in an adult case, and it seems likely that the prognosis would not be as good. The muscles of childhood have greater elasticity and would seem more suitable for such methods of passive stretching. The number of cases treated to date is small and the end-results may not be as satisfactory in a larger series of cases, but it is felt that no case of Volkmann's contracture in a child should be submitted to operation without at least a trial of conservative treatment.

Excision of the Femoral Head and Neck in Cases of Ankylosis and Osteoarthritis of the Hips

By J. S. BATCHELOR, F.R.C.S.

THE ankylosis of both hips which commonly follows ankylosing spondylitis is a most serious disability, for many of the patients so afflicted can neither walk nor sit. Provided the lumbar spine is supple most patients with bilateral hip ankylosis manage well if a moderate range of movement is obtained in one hip, but in ankylopoietics the rigidity of the spine which is almost invariably present makes a free and painless range of movement in both hips essential if treatment is to be effective. Such a result is best secured by an excision of the femoral head and neck.

The operation is performed through the Smith-Petersen approach. The junction of the femoral head with the acetabulum is first separated with a gauge and the femoral neck then divided low down flush with the trochanter with an osteotome. It is important that the opposing bony surfaces should be smooth, for irregular bony spurs or prominences may cause considerable pain when movement is commenced. After-treatment consists of traction to the leg by means of a Hamilton-Russell extension for two to three months. Hip and knee movements are commenced at the end of fourteen days.

The chief objection to this procedure is the potential instability of the resulting false joint. This disadvantage can be overcome to some extent by the use of a walking caliper for some months after operation, in order to allow the development of cicatrization around the joint. When both hips have to be treated, however, this is a tiresome process, and better stability can be easily achieved by a low subtrochanteric osteotomy of the Schanz type. The performance of this osteotomy, which can be carried out six to eight weeks after the excision, is facilitated by fixing the fragments with a plate which has been bent to the required angle beforehand (fig. 1). When both hips are being treated the angle of abduction of the distal on the proximal fragment should not exceed 35 degrees, otherwise difficulty may be experienced in adducting the legs to the neutral position.

As these patients have frequently been bedridden for years many months of treatment are necessary before the optimal functional recovery is achieved, and the end-result is sometimes marred by the associated knee stiffness which is often present. I operated upon my first case in 1938. After excision of both femoral heads, with an interval of six months between each operation, calipers were used for some months. A satisfactory degree of stability has been achieved for there has been no appreciable increase in shortening since the calipers were discarded, and the patient can do a full day's work and walk 4 or 5 miles with comfort. Since then 4 more cases have been treated, 3 by bilateral excision and 1 by unilateral excision. In 2 of the bilateral cases osteotomies have been performed on both hips. Of these 4 cases, 3 have a good range of painless movement in the hips and can walk with sticks. In the remaining case, in which a bilateral excision and osteotomy were performed in 1942, pain subsequently developed in one hip as the result of an irregular bony spur on the acetabular surface.

Although the numbers so far treated are small, I believe that excision followed by osteotomy is worth while in patients who are young and have a reasonable chance of returning to an active and useful life. In older patients, in whom the chief purpose of treatment is to restore hip movement so as to allow them to sit in comfort and walk about their homes, excision only is probably all that is required.

In unilateral osteoarthritis of the hip excision of the femoral head and neck is an accepted method of treatment. Here, however, the tendency to instability is greater than it is in those cases where ankylosis has been accompanied by surrounding soft tissue reaction and fibrosis. Although in some the use of a caliper gives satisfactory stability, this is by no means always the case and occasionally the resulting instability may cause considerable aching and discomfort. Excellent stability can be achieved by osteotomy, the distal fragment being abducted to an angle of 45 degrees with the proximal (fig. 2). This produces a slight abduction contracture of the hip and the resulting apparent lengthening of the leg compensates for some of the shortening.



FIG. 1.



FIG. 2.

The osteotomy can be performed six weeks after the excision and provided a plate is used no immobilization is necessary and the whole procedure does not take any longer to complete than an arthrodesis. In a small number of selected cases of osteoarthritis this combination of excision and osteotomy has given very satisfactory results.

Cases of Adolescent Kyphosis.—V. C. SNELL, F.R.C.S.

These cases were commented on by Miss M. FORRESTER-BROWN, M.D., M.S. They will be reported again at the Section for the Study of Disease in Children.

A sound film illustrating "Training for the Disabled" was shown by Mr. Stanley Evans.

Section of Proctology

President—R. S. CORBETT, M.Chir.

[July 18, 1945]

DISCUSSION ON THE MANAGEMENT OF THE PERMANENT COLOSTOMY

Mr. W. Ernest Miles: Very few doctors appreciate the value of the daily wash-out of the colon for controlling bowel movements. Consequently, when the patient leaves hospital and returns to his own surroundings he is left to his own devices as to the manner in which the wash-out is to be conducted. He seldom receives any instructions upon this important matter during his stay in hospital. There is no doubt whatever that bowel action can definitely be controlled by means of a daily plain water wash-out of one and a half pints (repeated if necessary) at a temperature not exceeding 80°F. as determined by the thermometer. Should the temperature exceed 80° inertia of the muscular coat of the colon is produced, resulting in retention of part of the fluid used and several hours may elapse before the muscular inertia disappears. A plain wash-out, if properly administered, can be relied upon to clear the colon completely of its faecal contents. In order that a patient may be able to carry out the wash-out in his own surroundings he should provide himself with the following articles: (a) A rubber rectal tube equal in size to a No. 20 English catheter; (b) a Higginson syringe; (c) a glass connexion which does not taper at one end; (d) a bath thermometer; and (e) a Miles' modification of the "Nitch" horn. It sometimes happens that difficulty is experienced in introducing the tube into the colon to the required extent. As a rule this is due to attempting to introduce the tube when the patient is sitting up or standing, or when he raises his head in order to pass the tube under the guidance of the eye and so puts his abdominal muscles on the stretch. In order to pass the tube, the patient should be recumbent with the abdominal muscles completely relaxed. One of the causes of difficulty in passing the tube is acute angulation of the colon at the point where it changes direction and passes forwards to the opening in the anterior abdominal wall. Such angulation can be entirely prevented by mobilizing the terminal portion of the descending colon.

Blind colostomy: By which I mean that a small incision is made through the abdominal wall at the site of the proposed colostomy and a loop of pelvic colon is hooked up by the finger and withdrawn from the pelvic cavity. Should the loop be protruded without tension, recession may not occur but if the sigmoid colon happens to be adherent to neighbouring structures, recession is certain to take place. It is for the above reasons that blind colostomy should never be performed. Should the "spur" recede it cannot prevent faecal matter from entering the cul-de-sac of the pelvic colon and forming a hard mass of faeces which may resemble a recurrent growth in the pelvis. As a result of the colon sliding through its peritoneal investment, altered peritoneal attachments between

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down urgently, to find him moribund, with a pelvic cellulitis, and peritonitis accompanied by an acute inflammatory condition of the scrotum and left groin; he died next day. The tube which was responsible for this catastrophe was a thick rubber tube about the size of an adult forefinger and had clearly been used with sufficient force to perforate the colon.

Incidence.—The incidence of an acute complication or mischance such as this is difficult to ascertain. Some patients would probably tend to be sent into their nearest emergency hospital or if living in remote districts and in the absence of operation or autopsy, the matter might pass unrecognized or not be reported to the surgeon who carried out the original operation. With the consent of my colleagues at St. Mark's Hospital, I have been able to collect 8 further cases of tube perforation which have occurred between 1937 and 1944.

Of these 8 cases, 6 were males and 2 were females; 6 were in connexion with terminal colostomies after radical excision of the rectum, 2 were left iliac loop colostomies. One case occurred while the patient was still in the hospital, the remainder were readmitted as emergencies at different times after discharge, varying from two days to the latest, which was about two and three-quarter years. The following is a brief report of a typical case.

The patient was a man aged 64 who made a good recovery after a synchronous combined excision of the rectum. On the day following his return home his wife did his wash-out; the fluid ran in well but did not all return; no discomfort was felt at the time. The district nurse then attempted a wash-out; his wife stated that some force was used and the patient complained of severe pain in the upper abdomen; later he became very shocked, with shivers and sweats. He had severe abdominal pain throughout the night. His doctor diagnosed peritonitis and sent the patient by ambulance to hospital. On admission he was moribund, cyanosed, pulse very feeble, pupils dilated. His abdomen was slightly distended, tender and rigid in left upper quadrant and generally below the umbilicus; peristalsis was absent and there was a slight watery discharge from the colostomy. He died half an hour after admission. Post-mortem examination revealed general peritonitis, and a small perforation was found on the mesenteric border of the colon, about 2 inches above the colostomy opening.

Mechanism.—The perforation usually occurs about 2 or $2\frac{1}{2}$ inches above the colostomy; if on the inner side the peritoneal cavity will be entered by the tube and gross contamination will result as the wash-out fluid is run in. Extra-peritoneal perforation may take place if the perforation is within the thickness of the abdominal wall or on the lateral side of the colostomy.

Various causes may be responsible for the perforation, such as the use of a large bore heavy tube or a tube made of hard inelastic rubber, and haste, inexperience and injudicious force in passing the tube. There may be local causes such as difficulty in passing the tube due to stenosis or the development of a subcutaneous colostomy bulge; in some cases no doubt the colon is unduly thin-walled and if diverticula are present, the point of the tube or catheter may become lodged in the thin-walled sac when only a slight amount of force might perforate it. In this connexion there is one point of interest, namely that all of these patients were over 60 years of age.

Signs and symptoms.—The characteristic feature is sudden acute abdominal pain either during or immediately following a colostomy wash-out, with collapse, vomiting and rapidly developing evidence of peritonitis. Sometimes the local signs are chiefly those of acute cellulitis round the colostomy, with redness spreading to the flank, perhaps with evidence of anaerobic infection and a thin offensive discharge from the colostomy. In 3 of these cases the hole in the colon could be felt with a finger.

Treatment.—Out of the 9 cases now reported, 8 proved fatal. The fatalities were comprised of 3 patients who were too ill for any surgical treatment and died of acute peritonitis within a short time; in 2 cases the lower 2 to $2\frac{1}{2}$ inches of the colostomy were excised in order to exteriorize the perforation, combined with pelvic drainage; and in 3 cases transverse colostomy plus pelvic or local drainage was effected, but in spite of all possible care they died, at times varying from a few days up to five weeks after the perforation had been sustained. Only one case survived; this was a man aged 72 with a loop colostomy and a well-marked colostomy hernia; in this case the perforation was clearly extra-peritoneal. The colostomy was excised and the loop withdrawn until the perforation was found in the proximal end $2\frac{1}{2}$ inches from the surface. The colostomy was re-established and the wound packed with sulphanilamide powder: drainage was provided through a stab incision on the lateral side.

In conclusion, I am opposed to the wash-out regime for colostomies for the following reasons:

(1) It is unnecessary, because the great majority of colostomy patients have a good intestinal function and with reasonable care and discretion in diet they achieve a satis-

the pelvic colon and the abdominal parietes are formed which must be divided before the loop of colon can be extruded sufficiently to create a satisfactory spur without undue tension. As a result too of general visceroptosis the angle created by the junction of the descending colon with the pelvic colon has gradually become acute, with the effect that it has become extremely difficult to hit off the passage-way into the pelvic colon for the purpose of introducing the tube. The treatment to be adopted is laparotomy.

A *weak spot* in the abdominal wall has been created by the passage through it of the loop of pelvic colon destined for the formation of the colostomy. In order to afford support to the weakened abdominal wall a well-fitting colostomy belt must be obtained. On no account should the patient allow himself to be persuaded to have a rubber bag attached to the cup of the belt to act as a receptacle for faeces. Such a bag creates suction and in the course of time the part of the colon which is proximal to the stoma is turned inside out and extruded through the stoma. It is important that the belt should be worn continuously when the patient is up and about.

Lastly, the stoma of a colostomy should be prevented from becoming stenosed by systematic dilatation. For this purpose the patient must be taught to pass his index finger to its full extent through the stoma. He must also be instructed how to pass his finger to its full extent before flexing the distal joint. As soon as the colostomy wound has healed firmly the index finger of the left hand (if the stoma is on the left side) should be passed through the stoma every day for a month, then once a fortnight for two months and finally once a month for six months, when it will be found that the tendency to contract has ceased.

Sir Charles Gordon-Watson: My remarks apply to a colostomy "in continuity" as distinct from "terminal". To secure a good working colostomy it must be well fashioned and it is first of all essential to secure a good spur by keeping the bowel outside the abdominal wall for at least three weeks by the use of a glass rod or other means, and also to avoid undue tension on the mesentery. The stoma should be well clear of the anterior superior spine to avoid interference with the belt. I prefer to make the opening through the split rectus. The size of the opening in the abdominal wall should be just large enough to allow a finger to pass down on either side of the glass rod. An ellipse of skin should be removed to prevent subsequent contraction which is apt to cause recession of the opening. All cups and bags should be avoided and a plain celluloid disc is all that is needed. Some patients find this unnecessary and wear only a singlet.

In the interval between operation and opening the colostomy, preferably about five days, I give paraffin daily which prevents unnecessary distension, and once opened, a good dose of castor oil. Subsequently the colostomy is trained to act only by a wash-out, which is given at the same time each day, using plain tepid water without soap and a flexible tube (size 14) which is passed up as far as possible with great care. Fluid is run in slowly, preferably by funnel, using a special apparatus of the Nitch type. It is important to ascertain the capacity of the colon in each case—which varies considerably—and to endeavour to fill the colon to start the reflex. Nurses must be specially trained for colostomy work. The horn in use then allows evacuation into a bucket. In private houses where the patients do their own wash-outs a special basin can be installed. It is important to train the patient to do his own wash-out before he leaves hospital, especially in the poorer classes who often prefer to wash-out in the evening. In hospital practice the almoner should be instructed to get in touch with district nurses in all colostomy cases.

When carefully carried out at the same time each day the colon learns to respond in an automatic way and many victims carry on with their work with little disability. In a small percentage of cases the colon will behave as if the stoma was the rectum and act regularly and automatically without a wash-out, with or without a mild aperient, and these patients are truly blessed. If there is a tendency to looseness disasters are liable to occur. One to three teaspoonfuls of visiblin, isogel or similar preparations given at night will keep the motions firm. If the motions are offensive Kerol capsules should be given.

Mr. W. B. Gabriel: After a colostomy has been established, whether it is a terminal or a loop colostomy, whether left iliac or transverse, we have to decide if the bowel is to be allowed to act naturally or whether the wash-out regime is to be adopted. My opposition to colostomy wash-outs was determined about fifteen years ago by the following case.

The patient was an active old man of over 80, with an inoperable carcinoma of the rectum causing chronic obstruction. I did a left iliac loop colostomy from which he made a good recovery and reached the convalescent stage, but three weeks later I was called

How then are we to attain but one bowel action a day for a colostomy?

The answer is by routine morning wash-out if the rhythm does not come naturally after a short trial. A bowel completely emptied by a wash-out followed by a morning bath and clean dressings enables a man to face the day and his fellows without handicap.

"If we command the morning we command the day" is a true and wise saying.

The colostomy is likely to be regular after the removal of the rectum if the daily evacuation before colostomy was by rhythm rather than "feeling".

Mechanism of the colon.—To know some facts about the physiology of the large gut helps in the advice and management of the colostomy. The feces reach the colon from the cæcum in soft isolated masses. These masses are compressed into larger masses and become firmer by water absorption. Here they are stored till mass peristaltic action empties the bowel and leaves storage room for the next twenty-four hours' accumulation.

If the nerve mechanism of the colon is damaged the functions* of storage, mass formation and the twenty-four-hour peristaltic rhythm are changed. Continuous passage of "pellet" feces then takes place.

A simple fact forgotten by aperient addicts is that the colon was made for solid feces and is fully provided with mucus for lubrication by myriads of mucus-secreting glands.

The colon's chief function is unconscious storage between evacuations. Unconscious mass peristalsis empties the colon into the conscious rectum or out through the colostomy if present.

Peristaltic waves can be excited or prevented by factors which the patient should know. Aperients ruin regular rhythm and frustrate the bowel storage mechanism by changing solid into liquid feces. Unsuitable diet both in amount and quality can disturb the storage mechanism. Emotional states will not be forgotten in this respect by the present generation for the aperient effect of the air-raid alert is known to many.

To promote the emptying peristaltic waves at the right time there should be the morning ritual of regularity preferably after breakfast, the right position of the body and the purposeful unhurried unanxious time. It is curious that many teach this ritual to their children but fail to carry it out themselves.

Attitude to colostomy.—The surgeon and nurse can inspire the patient to have the right mental attitude. Patience above all is required to make life normal again. Resentment against misfortune, fear of the disease or accidents, self-pity, or self-absorption can then be replaced by confidence and an outward purpose in life.

Unfavourable social environment can be an obstacle to the right attitude to colostomy. In two cases I neglected to inquire into their amenities for attention to the colostomy. They both committed suicide for they had no home and lived a wandering life in lodging houses. It taught the lesson that a person must have privacy and suitable conveniences in a home or he should be in a hospital.

Tube insertion.—Unlike the colon the rectum is capacious and a tube inserted can curl if impeded by folds and curves. Its walls are strong by reason of the longitudinal muscle which here spreads. It is supported by the walls of the pelvis, the sacrum and the close surrounding viscera. None of these things obtains in colostomy. There is the danger of perforation with a rigid tube. A thin tube No. 12 English rubber catheter inserted with gentleness will prevent the misfortune of perforation.

Mr. Rupert S. Corbett: *The management of a permanent colostomy.*—Let us consider the subject under two headings: (1) *The part played by the patient.* (2) *The part played by the surgeon.*

From the point of view of the patient, he wants a regular evacuation of the bowel and freedom from the anxiety of leakage. He wishes to be able to carry on his daily life in much the same way as he was accustomed to do before the operation.

His part in the management can be carried out in one of two ways:

(a) A daily action of the colostomy by training the bowel to act regularly of its own accord.

(b) Regular daily wash-outs of the bowel.

There is no doubt that if we leave it to Nature—provided Nature plays safe!—the former (a) is the ideal, and every patient should be given a chance to establish this course.

Daily wash-outs, on the other hand, bring about a feeling of safety and security which the patient appreciates so much and which many of us feel should not be denied him.

factory and regular rhythm with formed colostomy actions. Only rarely do we meet with patients who are troubled by irritability of the colon, and this is best treated by administration of kaolin, kaldrox or chlorodyne, together with special care in the restriction of roughage.

(2) It is *harmful* because it is not natural for the colon to have any solution thrust into it daily, whether it be plain water, normal saline or soap and water. Colonic lavage for prolonged periods induces a chronic catarrh of the colon with a hyperemic mucosa, a contracted bowel lumen and excessive formation of mucus; in other words this routine induces a state of catarrh and irritability in the colon which is exactly contrary to what is desirable after a colostomy.

(3) It is *dangerous* because the passage of a tube up the colostomy may lead to perforation, peritonitis and death. If we instruct or allow patients, their relatives or nurses to wash out colostomies we are inviting this catastrophe, and in my opinion routine colostomy wash-outs should be abandoned. In hospital work a colostomy wash-out is only rarely necessary in the immediate post-operative period, and usually insertion of a glycerine suppository serves the purpose equally well.

Summary.—Nine cases of tube perforation due to colostomy wash-outs have been collected, and of these eight proved fatal. All of these cases occurred in patients over 60 years of age. If colostomy wash-outs are considered to be essential in such cases it is necessary to advise and teach those concerned that the greatest care and gentleness are necessary, and that only soft pliable rubber catheters should be used.

Mr. E. T. C. Milligan: *Mucus secretion and dressings.*—When mucus-secreting rectal mucosa was to be joined to hairy gland-containing skin of the anus, a difficulty had to be overcome if we were to be unconscious of our body, for the skin of the anus is very sensitive to moisture, and reacts violently to irritation. The difficulty was overcome by lining the anal canal with mucosa which had dropped its mucus-secreting glands, and with anal skin which had lost its hairs and glands. These glandless linings were joined together in an irregular line—the muco-cutaneous line inside the anal canal. Thus no bowel mucus escapes from the anus. When the mucus-secreting colon is joined directly to the skin of the abdominal wall as in colostomy, there is no intervening non-secreting lining, nor controlling muscle to prevent the escape of mucus: so an absorbent dressing must be worn to protect the clothes. Fortunately the skin of the abdomen is not sensitive to moisture or irritation as is the skin of the anus.

Weakness of colostomy incisions and belt support.—The natural emergence of the bowel through the musculature of the perineum makes provision against weakness and provides neuromuscular balanced control. How different with the colostomy so rudely made through the abdominal muscles. There results an inevitable weakness and hernia occurs from time to time; especially in colostomy in continuity, the so-called spur colostomy. To control and prevent this weakness a firm elastic disc is worn in the colostomy belt. Cups and receptacles encourage the development of herniæ. Repair of the herniæ is rarely needed nor need strangulation be feared.

No surgical substitute for the rectum.—The surgeon cannot yet provide a substitute for the rectum. The rectum is under the control of the patient for storage and ejection. A colostomy can never be trained to have conscious sensations or voluntary powers similar to the rectum. The crude muscles of the abdominal wall cannot act like the specialized rectal and anal muscles in retention and expulsion.

Bowel-rhythm obtainable.—The same rhythm or regularity of bowel action can be attained with a colostomy as with a normal rectum; that is the twenty-four hour rhythm, for in all of us with or without a rectum this rhythm depends on the colon.

Put as a dictum: "We cannot control the colostomy but it can be controlled."

Nature's standard of one and only one motion a day can be reached with a colostomy. It is important that the surgeon, nurse and patient be resolved to attain this standard. It is found on questioning patients that they are pleased with two or three actions per day; indeed patients can be satisfied with very low standards in this respect. Only by inquiry can the state of things be discovered and altered. If the colostomy act more than once a day the feces are carried about in the dressings. There is a sense of insecurity, the mind is unduly centred on the abnormality of function, and it is unpleasant for associates and friends. The insecurity will restrict activity and narrow life.

The same freedom that comes from normal function with a rectum can be experienced with a colostomy. It may be a battle to get it. Time and patience are needed as well as team work between patient, nurse, friends, and surgeon.

How then are we to attain but one bowel action a day for a colostomy?

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Daily wash-outs, on the other hand, bring about a feeling of safety and security which the patient appreciates so much and which many of us feel should not be denied him.

There are difficulties and dangers in adopting this course, but we have heard of ways and means to overcome them.

I need only refer to:

(1) The use of a small soft red rubber catheter to reduce the chance of perforation. (2) The avoidance of too warm solution which soothes rather than stimulates the bowel to act. (3) The use of an outfit for irrigations and control of drainage of the colostomy. (4) The patient should not be tempted by the instrument maker to fit a bag or cup over the colostomy—just in case it should leak! The cup produces suction and prolapse is the result. A disc held in place by a light belt is considered the right thing to advise. (5) The cul-de-sac should be washed out once a week. (6) Diet and aperients: A recent writer has said "Colostomy management begins in the kitchen". The patient will find what suits him best. A good breakfast in bed has been recommended. Aperients: Not usually necessary. Petroleum emulsion can be used.

The part played by the surgeon.—It is of great importance that certain essentials should be remembered in the formation of the colostomy and in the management of the post-operative period. They lead to easy management and avoidance of complications.

(1) *Position of stoma.*—Choice of three positions: Left iliac, rectus sheath, and possibly epigastrium. Colostomies in all positions appear to work equally well:

Left iliac position: Avoid bringing out the bowel too near the anterior superior spine. It interferes with the subsequent fitting of the disc under the belt.

The rectus incision is apt to lead to herniation of the abdominal wall when used as the exploratory incision as well.

Ventral hernia is common, especially in the lower abdomen. It is more likely to occur where the exploration of the abdomen is carried out through the same incision that forms the colostomy. There are many points therefore in favour of two incisions, e.g. a right paramedian incision for the exploratory and a gridiron for the colostomy.

To obviate stenosis of the colostomy, which favours herniation, excision of a portion of skin as advised by Miles is of considerable value.

(2) *The formation of an adequate spur.*—This is referred to by all as an essential. A glass rod is popular, easy to apply and very satisfactory. The rod or its substituted rubber tube remaining in situ for three or four weeks.

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Opinions are divided. There is no doubt that delayed opening favours a paralytic ileus. Also it may prevent adhesions of the colostomy to the abdominal wall. No ill-effects seem to occur if the colostomy is left closed for three to five days. The risk of sepsis is reduced and frequently stasis is passed over the closed loop and so prevents distension which would favour ileus or prolapse. It appears therefore that it is safer, though not imperative, to open the colostomy at once.

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(2) *Social condition of the patient.*—This must be remembered as there is no doubt that in the case of a few a colostomy is nothing short of a tragedy, as Milligan has said. For the unmanageable case or the patient who is going steadily down hill there is a crying need for convalescent homes that will take colostomy cases.

Section of the History of Medicine

President—Sir ARTHUR MACNALT, K.C.B., M.D.

[May 2, 1945]

Wilhelm Conrad Röntgen (1845-1923) and the Early Development of Radiology

By E. ASHWORTH UNDERWOOD, M.A., B.Sc., M.D., D.P.H.

THE year 1945 is associated in two ways with the life and work of the great physicist, Röntgen. Since he was born on March 27, 1845, it is the centenary year. His greatest discovery was made on November 8, 1895, just fifty years ago. The present time seems opportune to review his work and to remember, in passing, those other pioneers who made his discovery possible.

The production of X-rays depends essentially on the fact that when an interrupted current of electricity is passed through a vacuum tube, a stream of rays—the cathode stream—flows from the cathode. The cathode stream can be bent by a magnet. Where it impinges on another body, the glass of the tube or a specially prepared anode, X-rays are produced. In nature and properties these are essentially different from cathode rays. In short, before any advance could be made in the discovery of X-rays, two operations had to be practicable—the production, first of a good vacuum, and second of an interrupted electric current. It is strange that both of the appliances necessary were discovered by the same man—Otto von Guericke of Magdeburg—and were published in the same book.

Guericke (1602-1686) was born in Magdeburg and studied mathematics and mechanics. He was a practical man of the world, and he worked on the fortifications of the fortress. He did not publish his celebrated book until he was 70 years of age, and the date of the invention of the air-pump is therefore uncertain. It was probably between 1635 and 1645. He first used wooden casks and later a copper sphere, which collapsed when a certain degree of exhaustion had been reached. Guericke demonstrated his results before the Imperial Diet at Ratisbon in 1654. The demonstration took first the form of a proof that after exhaustion thirty horses were required to pull the spheres apart; and secondly, an estimation of the actual force required to effect separation. Guericke proved conclusively by this method that air has weight, and he was able to make a rough guess at its density. Since his results were not then published, we have to turn to another source for the first description of his apparatus—the *Mechanica Hydraulico-Pneumatica* of Gaspar Schott (1608-1666) published in 1657 [4]. Since Schott was Professor of Physics and Mathematics at Würzburg, there is a coincidental connexion between the inventor of the air-pump and the man who made the most fruitful use of it. In England Robert Boyle (1627-1691) became interested in the air, and his air-pump was an improvement on that of Guericke. The result was his well-known monograph on *The Spring of the Air* (1660) [5], which had important results in many fields. Stimulated by Boyle's developments, Guericke later made a third air-pump, which was a great improvement on his previous models. His results were published in his great work, *Experimenta Nova (ut vocantur) Magdeburgica de Vacuo Spatio* (1672) [6]. In this Guericke also described his frictional electric machine. This consisted of a large glass globe which was filled with molten sulphur. On cooling the glass was removed, and the sulphur sphere was rotated by hand. His work in the field of the induction and conduction of electricity was very important, and again he had a marked influence on Boyle's future experiments.

There are difficulties and dangers in adopting this course, but we have heard of ways and means to overcome them.

I need only refer to:

(1) The use of a small soft red rubber catheter to reduce the chance of perforation. (2) The avoidance of too warm solution which soothes rather than stimulates the bowel to act. (3) The use of an outfit for irrigations and control of drainage of the colostomy. (4) The patient should not be tempted by the instrument maker to fit a bag or cup over the colostomy—just in case it should leak! The cup produces suction and prolapse is the result. A disc held in place by a light belt is considered the right thing to advise. (5) The cul-de-sac should be washed out once a week. (6) Diet and aperients: A recent writer has said "Colostomy management begins in the kitchen". The patient will find what suits him best. A good breakfast in bed has been recommended. Aperients: Not usually necessary. Petroleum emulsion can be used.

The part played by the surgeon.—It is of great importance that certain essentials should be remembered in the formation of the colostomy and in the management of the post-operative period. They lead to easy management and avoidance of complications.

(1) *Position of stoma.*—Choice of three positions: Left iliac, rectus sheath, and possibly epigastrium. Colostomies in all positions appear to work equally well:

Left iliac position: Avoid bringing out the bowel too near the anterior superior spine. It interferes with the subsequent fitting of the disc under the belt.

The rectus incision is apt to lead to herniation of the abdominal wall when used as the exploratory incision as well.

Ventral hernia is common, especially in the lower abdomen. It is more likely to occur where the exploration of the abdomen is carried out through the same incision that forms the colostomy. There are many points therefore in favour of two incisions, e.g. a right paramedian incision for the exploratory and a gridiron for the colostomy.

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Francis Hauksbee (the elder, d. ? 1713) who had already effected considerable improvements in the air-pump, began to experiment in 1705 on the effect of agitating mercury in a vacuum, and later on the results produced by rubbing together various bodies in a receiver wholly or partially exhausted of air. His experiments were described in the *Philosophical Transactions* as they were completed. In 1709 Hauksbee collected his experiments and included the description of his air-pump and other apparatus in his *Physico-Mechanical Experiments* [7]. In his first experiment Hauksbee placed some mercury in a glass vessel which was enclosed in a large receiver. A glass tube passed from the stop-cock of the receiver and opened under the surface of the mercury. The receiver was partially exhausted of air; the stop-cock was then opened, so that the air rushing down the tube, forced the mercury violently up against the sides of the receiver. "In this confusion and hurry of its Parts it gave, all round, the appearance of Fire; it look'd like one great flaming Masse, compos'd and made up of innumerable little glowing Balls." Hauksbee was therefore the first to produce an electrical discharge in a vacuum. In his second experiment Hauksbee noticed that none of the mercury "appear'd luminous, but what was contiguous to the sides of the Glasses in its descent"—surely a very pertinent and important observation. In these experiments he obviously thought that the luminosity was a property of the mercury, and hence he termed it "mercurial phosphorus". He studied the effect of different degrees of exhaustion of the air on the quality of the light produced, and he differentiated between the light produced in the open air and in a partial vacuum. Hauksbee further showed that even light friction caused by placing the hand on a revolving glass globe partially exhausted of air would produce luminosity in the globe. The quality of the light altered rapidly when the air was readmitted suddenly, but only slightly when the air entered slowly. By rubbing together amber beads and wool in an exhausted globe he obtained a luminosity, which he says

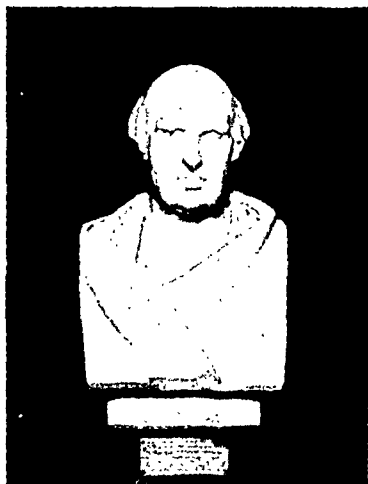


FIG. 1.—Bust of William Morgan, by Joseph Towne. Exhibited in the 1834 Exhibition of the Royal Academy, and now in the possession of the Equitable Life Assurance Society. Photograph by Mr. J. G. Anderson, from whose book (9) it is reproduced by permission.

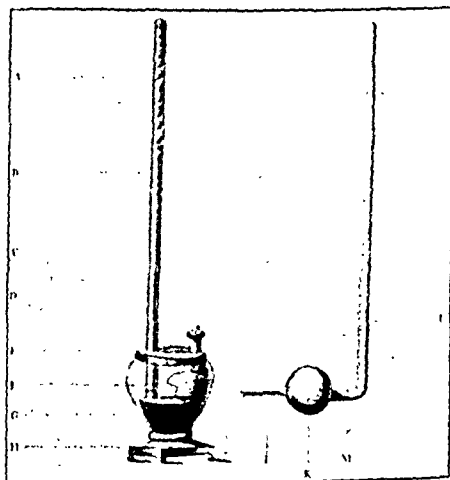


FIG. 2.—Morgan's Apparatus.
(Reproduced by permission of the Royal Society.)

was "not a meer lambent Fire, but such as is accompanied with great Heat". In the same way he tried rubbing together glass and wool, glass and glass, glass and oyster-shells, oyster-shells and wool. This brief summary must close with the statement that Hauksbee realized quite clearly that the phenomena were dependent upon the existence of a partial vacuum, and he possibly suspected that they were electric in nature. The experiments of Hauksbee were extended about 1740 by the Abbé Nollet (1700-1770) who connected an electrical machine to a vacuum by means of a chain. He demonstrated that electrification could occur in a vacuum, but otherwise his results do not take us very far.

The next date of importance which I have been able to discover is 1785. Between 1740 and 1785 there were possibly others who contributed something, but I have found no papers bearing on this subject in the *Philos. Trans.* or in certain other journals of the period. In 1785 William Morgan published certain experiments in the *Philosophical Transactions* which are of great importance, and which moreover are little known [8]. Morgan (1750-1833) (fig. 1) was one of the greatest, perhaps the greatest, of actuaries. He was born in Bridgend, Glamorgan, and he was apprenticed to a London apothecary, according to the *Dictionary of National Biography*. Mr. J. G. Anderson, who has dealt fully with his actuarial activities, says that he qualified as a doctor from Guy's Hospital. At the age of 24 he became assistant actuary, and in the following year chief actuary to the Equitable Assurance Society, and he retained this office until his eightieth year [9].

Morgan's writings are mainly actuarial, but in 1785 he had a short physical paper published in the *Phil. Trans.* This paper was entitled "Electrical Experiments Made to Ascertain the Non-conducting Power of a Perfect Vacuum". The apparatus (fig. 2) consisted of the following: A mercurial gauge (B) about 15 inches long was carefully boiled until every particle of air was expelled from the inside, and was coated with tin-foil to a distance of 5 inches from its sealed end (A). It was inverted into mercury through a perforation (D) in the brass cap (E) which covered the mouth of the cistern (H). The whole was cemented together, and the air was exhausted from the inside of the cistern through a valve (C) in the brass cap. A small wire (F) was fixed on the inside of the cistern, connecting the brass cap with the mercury (G) in the cistern. The coated end (A) of the gauge was then applied to the conductor of an electrical machine. With this apparatus Morgan showed that, if the tube was completely exhausted, no light could be produced from it. When only a minute portion of air is admitted the resulting light is of a beautiful green colour. As more air is admitted the colour changes to darker shades and finally to indigo or violet. Morgan suggested that in an almost perfect vacuum the particles of air may be so far separated from each other that they are not able to transmit the electrical fluid, but if air is admitted and the particles are brought within a certain distance of each other, their conducting power begins and increases till it reaches its limit. Morgan also used a fine thermometer tube, and in this way he obtained a spark 42 inches long. When a bulb was blown at the sealed end, the light filled the whole of it and then passed through the tube as a spark. Such bulbs break readily after the passage of a few charges, and this may have been the reason why Morgan's experiments were not repeated by others.

Although Hauksbee had shown that in a partial vacuum an electrical charge can pass in the form of a luminous discharge, Morgan's contribution was to demonstrate clearly that the colour of the light rays depends on the degree of exhaustion—that is, the quality of the rays depends on the hardness of the tube. It would seem to be fitting to term this relation *Morgan's phenomenon*. It should also be said that Morgan prepared his apparatus with the greatest of care, in order to obtain what he considered to be a perfect vacuum. To this end he even boiled the apparatus and the mercury, and he therefore was the first to obtain what later came to be called a "Coolidge vacuum".

I must pass over almost without comment the work of Faraday, Hittorf, Goldstein, Hertz and others. Faraday observed the dark space round the cathode, which led Hittorf to the recognition that in a discharge through a partial vacuum the rays pass from the cathode. Goldstein in 1876 introduced the term "cathode stream". Seven years previously Hittorf had shown that obstacles placed in this stream cast a shadow on the glass tube. Varley and Crookes showed that the cathode stream was deflected in a magnetic field, and that the rays consisted of electrified particles shot out from the cathode. In 1892 Hertz showed that these rays could penetrate thin gold leaf or aluminium, and similar work was done by Lenard. At the time when Röntgen began his researches the tubes devised by Hittorf, Lenard and Sir William Crookes respectively were commonly employed in experiments of this type [10].

Mention should also be made of the work of Sir Herbert Jackson (1863-1936) on the focus tube, which was originally devised by him in studying the exposure of fluorescent material to the electrical discharge in vacuum tubes. Sir William Crookes appears to have discovered the focusing effect of a concave cathode in 1874, but Jackson was the first to adopt this design for practical purposes, and he found that concave cathodes serve to restrict the area of the phosphorescent material. In January 1894 he made a discharge tube fitted with a concave aluminium cathode and an inclined platinum anode. This was the original Jackson "focus tube". With it, like other early workers, he undoubtedly obtained X-rays, but he considered that the rays which were emitted from the anti-cathode were long wave ultraviolet radiations. Jackson used his tube, of course, as a source of light for his fluorescence experiments, but immediately after the announcement of Röntgen's discovery in January 1896 he was able to use his original tube for X-ray work. On May 6, 1896, he demonstrated the use of this tube at a *Conversazione* of the Royal Society, and in the descriptive catalogue of this function he expressly says that the tube is "a slight modification . . . of a tube originally introduced by Mr. Crookes". In his obituary of Jackson Dr. Harold Moore [11] says of his work that, "had the observations been viewed from a different standpoint, Röntgen's discovery might have been considerably anticipated. At no time, however, did Sir Herbert Jackson advance any claim to be the original discoverer of X-rays, or countenance any suggestion that such a claim might be made on his behalf. . . . He expressly stated on several occasions that the characteristic penetrating power of the radiations emitted by the anti-cathode was neither discovered nor suspected by him". At this time Jackson was working with Mr. D. Northall Laurie, and many X-rays were taken which do not seem to have survived. Mr. Laurie has, however, shown me a number of X-rays which he himself took early in 1897, still using the original Jackson focus tube, an Apps coil with 5 inch spark, and an eightfold secondary battery.

RÖNTGEN'S EARLIER LIFE AND WORK

It was in late October 1895 that Röntgen entered the field. Like so many others who have scaled the academic heights, his approach to these glittering summits had been somewhat unorthodox, and before considering the events of that pregnant autumn, it would be well to glance at the man, his nature and his nurture. This is especially desirable since he is too near our own time to find more than passing, though

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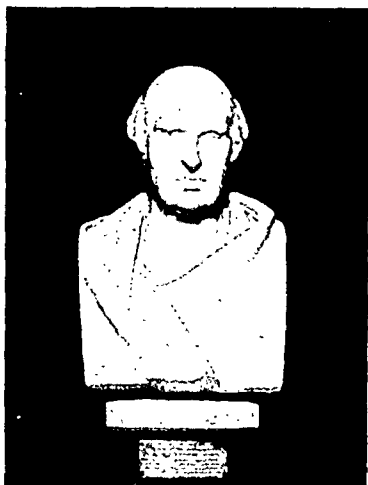


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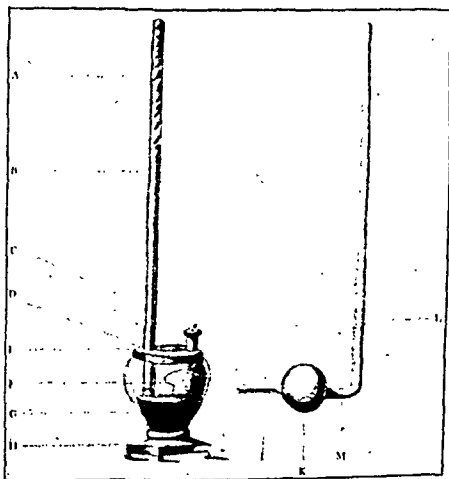


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THE DISCOVERY OF X-RAYS

It was in this favourable environment that Röntgen started to work on cathode rays in late October 1895. He used a Ruhmkorff induction coil, a mercury interrupter, and a Hittorf-Crookes vacuum tube [13]. He had also been working with Lenard tubes, which were covered with black paper, in which a window was cut for the passage of the cathode rays. Fluorescent screens were the usual method of testing for the cathode rays even at that time. At a late hour on Friday, November 8, when there were no assistants in the laboratory, Röntgen was testing the density of the black cover—without a window—fitted over a Hittorf-Crookes tube. As he told an interviewer, the shield was impervious to any light known. He noticed bright fluorescence in a screen of barium platino-cyanide which lay on a bench nearby. It seemed improbable that the effect could have been produced by cathode rays as their nature was then understood; but in order to exclude them he experimented with a screen at a greater distance than the known range of cathode rays—even up to 2 metres. The fluorescence persisted. The next step was to interrupt the rays by various bodies which would have been quite opaque to cathode rays. In this way he deduced that he was dealing with a new kind of radiation, the penetrating power of which varied roughly with the density of the interrupting body. When his hand was the interrupting body, he saw the shadows of the bones upon the screen. The next step was to replace the screen by a photographic plate. The first X-ray photograph—frequently reproduced since then—was that of Mrs. Röntgen's hand.

There followed seven weeks of intensive work, during the early part of which Röntgen slept and ate in his laboratory. According to his wife, he was morose and abstracted, and resented the intrusion of mundane matters. On December 28 he presented to the President of the *Physikalisch-Medizinische Gesellschaft* of Würzburg his first written report on the discovery. This he termed a "Preliminary Communication" (*Vorläufige Mitteilung*). It is often said that Röntgen read this report before a meeting of the Society, but this statement is incorrect [14]. Owing to the Christmas season there were no meetings. Because of its importance, however, the report was accepted for immediate publication in the *Proceedings* (*Sitzungsberichte*), and it was printed a few days later. The report was entitled "On a New Kind of Rays" (*Eine neue Art von Strahlen*) [15]. On January 6 the news was cabled from London to the whole world, and the reaction was immediate. It should be noted that Röntgen made no oral communication on the subject until January 23, when he addressed the *Physikalisch-Medizinische Gesellschaft* with von Koelliker in the Chair.

In his Preliminary Communication Röntgen presented the subject already fully fledged. He proposed to call the new rays "X-rays" in the meantime. He noted that fluorescence occurs whatever side of the test paper is turned to the tube, even up to a distance of 2 metres. He classified various substances according to their transparency, and he distinguished between the two types of glass. Lead in a thickness of 1.5 mm. is practically opaque. He then investigated the problem of refraction of the rays, using mica prisms containing water or carbon bisulphide, and also prisms made of hard rubber or aluminium. He thought there might be slight deviations. Lenses he found to have no action. Regular reflection does not take place. Bodies behave to the X-rays as turbid media do towards light. He considered that X-rays move with the same velocity in all substances.

He then compared the X-rays with cathode rays. Air absorbs a far smaller fraction of the X-rays than of the cathode rays. A characteristic of the cathode rays is that they can be deflected by a magnet, and he stated that he had made many unsuccessful attempts to show deflection of the X-rays by this method. There follows the important observation that the X-rays proceed from the spot where the cathode rays strike the glass wall of the tube. If the cathode rays are deflected by a magnet, it is observed that the X-rays proceed from another spot. Hence, since X-rays cannot be deflected, they cannot be identical with cathode rays. The production does not take place in glass alone, but also in aluminium.

Röntgen then mentioned some of the shadow-pictures which he had observed or photographed. Amongst the best known are the set of weights in a closed wooden box; the human hand; the shadow of his laboratory door; a compass in which the magnetic needle was entirely enclosed by metal; and a piece of metal whose lack of homogeneity became noticeable by means of the X-rays. This photograph of a specimen of metal is the source of all our uses for X-rays in metallurgy. Finally, Röntgen hazarded the tentative suggestion that X-rays are longitudinal vibrations in the ether.

The first translation of this epoch-making paper to appear was published in *Nature* on January 23. On February 8 it appeared in French in *L'Éclairage Électrique*, and again in English in the American journal *Science* on February 14.

very honourable, mention in the histories of science, and since moreover he is sufficiently distant for the softening of the contours which the years bring in their train.

Wilhelm Conrad Röntgen was a Rhinelander, a native of the little town of Lennep in Bergischen, where he was born on March 27, 1845. His father was a merchant, and father and mother were first cousins. His mother was really Dutch. When Röntgen was 3 years old the family moved to Apeldoorn, and there, at the Institute of Martinus Herman van Doorn and in the streets, he added Dutch to his native German. Many years later he brushed up his Dutch in order to greet an old colleague at an official celebration in Holland. He was expelled from the school because of his refusal to split on a fellow pupil who had drawn a caricature of the teacher. This was a serious matter, since it deprived him of the opportunity for matriculation. After a period at the Technical School at Utrecht he did indeed enter the University—but not as a regular student. He was then nearly 20 years of age. Conditions were easier at Zürich, and in the same year he passed his entrance examination and migrated to that beautiful city. He took his diploma in mechanical engineering in 1868, and his degree of Doctor of Philosophy in 1869 at the age of 24, and before he had finished his course fell under the spell of Kundt, to whom he became an assistant. Two years later he followed Kundt to the University of Würzburg, and in the following year to Strassburg. In 1875, at the age of 30 years, he became Professor of Physics and Mathematics at the Agricultural Academy of Hohenheim in Württemberg.

It must have been clear to Röntgen's associates that he would not be satisfied with a chair in a second or third class institution. It was obvious that his technical ability, his facility for carrying out complicated experiments with apparatus devised by himself and made with his own hands, and his deep theoretical knowledge of physics were worthy of higher things. If he had started his university career badly, he now took the right step. In 1876, after a year at Hohenheim, he returned to Strassburg as the associate professor with Kundt. During the six years which elapsed between his first arrival at Strassburg and the date of his leaving, he published fifteen papers—the last three with Kundt. In 1879, when he was 34 years of age, he was called to the Chair of Physics at Giessen. There he spent nine happy and fruitful years. In 1888 the University which, although he had occupied a post on its staff, had refused to grant him full academic status because of his unorthodox entry to his academic career, honoured him by offering him the post of Professor of Physics and Director of its new Physical Institute. In that year he removed to Würzburg with his wife—a relative of Otto Ludwig, the poet, whom he had married in 1872—and there they occupied the apartment on the top floor of the Institute. This Institute is of particular interest to all who are connected with radiology, since it was there that X-rays were discovered by Röntgen seven years later.

During his twelve Würzburg years Röntgen was certainly at the height of his ability as an experimental physicist. He was thoroughly at home in the Würzburg atmosphere, and in 1894 he was Rector of the University. From the personal reminiscences given by Fräulein Boveri [12]—daughter of his friend Theodor Boveri, the zoologist—and others, it would appear that his department was well organized, and he had few academic worries—except possibly the necessity of teaching, which appealed to him less as the years passed. He spent much time in outdoor pursuits, especially hunting and botanizing. Each year he took holidays in the Alps—for example at Pontresina—and also at Lake Como. In later life he acquired a hunting lodge at Weilheim in the Bavarian Alps, which he equipped with a satisfactory scientific library.

Some consider that, even if Röntgen had not discovered the X-rays, he would have been one of the greatest scientists of the nineteenth century, but there are various views on this point. I have read a number of his other papers, but am not qualified to express an opinion. Of his previous work, especially notable were his experiments with Kundt at Strassburg on the electromagnetic rotation of the plane of polarization of light in gases. Faraday had attempted to demonstrate this phenomenon, but had been unsuccessful. He had also written on the absorption of heat in water vapour, the compressibility of liquids and solids, and the production of magnetic effects in a dielectric—the latter investigation being ranked by him as equally important as his discovery of the X-rays. He thus discovered the Röntgen current, which led later to the theories of Lorentz and of relativity. Finally, throughout his career he wrote many papers dealing with crystals, which probably influenced later investigators, and especially von Laue, Friedrich and Knipping in their determination of the nature of X-rays in 1912. It is worthy of passing note that in 1877 Röntgen contributed a short paper to *Nature* entitled "A Telephonic Alarm".

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It would seem that the attitude of the popular Press had much influence on the future development of the new methods. Journals in all countries had comments and jokes on the X-rays, and these served to make people interested, and stimulated them to ask their physicians to take X-ray pictures if they were in doubt. These comments often illustrate the misconceptions to which I have referred. For example, early in 1896 a photographer sent a customer an X-ray picture of a needle embedded in a human foot. He received the following reply: "Photograms received, very tame. Send more sensational ones, such as interior of the belly, backbones, brains, liver, kidneys, head, lungs, &c." By June a Miss Willard, a prominent temperance worker in the United States, was saying: "I believe the X-rays are going to do much for the temperance cause. By this means drunkards and cigarette smokers can be shown the steady deterioration of their systems, which follows the practice—and seeing is believing!" There was obviously a belief that some sort of waistcoat pocket X-ray apparatus might be developed, and a progressive London firm even advertised X-ray-proof underclothing. An Assemblyman from New Jersey actually introduced on February 19, 1896, a bill into the House at Trenton, N.Y., "prohibiting the use of X-rays in opera glasses in theatres". The same idea is expressed in the delightful cartoon in *Punch* of March 7, 1896.

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As has already been mentioned, the first X-ray photograph of the human body taken in this country by Röntgen's method was made by Mr. A. A. Campbell Swinton and Mr. G. Stanton in the second week of January 1896. The exposure was four and a half minutes [27]. According to Pullin [3], Swinton's first X-ray of the human hand was made on January 7, the day after the announcement of the discovery by Röntgen, and the exposure was twenty minutes. It was reproduced in *Nature* on January 23, was demonstrated at the Physical Society on January 24, and on February 13 at a lecture before the London Camera Club. By January 25 Swinton had announced that lantern slides of this X-ray were available, and shortly afterwards he opened a laboratory for X-ray work in Victoria Street. By February 1 Neusser in Vienna had obtained X-rays of gall-stones in the gall-bladder, and a calculus in the urinary bladder. The *Lancet* was now proclaiming that English investigators must not be behind their co-workers abroad in the practical application of the discovery. Dawson Turner in Edinburgh showed a series of X-rays on February 5. One of the first surgical applications to be reported was that of a bullet in a boy's wrist, treated and written up by Sir Robert Jones and Sir Oliver Lodge [28]. On February 24 Sydney Rowland, of St. Bartholomew's Hospital, gave a demonstration before the Medical Society of London. Hall, Edwards in Birmingham had localized a needle and a bullet by means of the X-rays; he also produced an X-ray of a vertebral column. At Aberdeen MacKenzie Davidson had also carried out similar work by the middle of February. Silvanus Thompson, Oliver Lodge, Schuster and other great physicists were taking much interest in the application of the method to medicine, and Silvanus Thompson soon became the first President of the Röntgen Society. One of the most energetic of the early British workers was Dr. John MacIntyre of Glasgow, who was the pioneer of fluoroscopy by means of his cryptoscope. In addition to his abundant work on the bony structure of the limbs, he obtained distinct shadows of the vertebral column and ribs [29]. By April for his cryptoscope he was using calcium tungstate, which had been recommended for this purpose by Edison after tests on eighteen hundred substances [30]. Edison himself probably first used the stereoscopic screen. In examining the antrum of Highmore MacIntyre tried putting small X-ray tubes in the mouth, and the screen outside. He paid great attention to the degree of hardness of his tubes, and he sometimes kept the air-pump connected in order to obtain a correct vacuum [31]. He pointed out that a tube can be restored to its correct condition by the use of a Bunsen burner. In November 1896 MacIntyre was the first to use a succession of X-ray pictures of moving objects, viz. a frog's leg in motion [32], and he was also the first to devise the method of photographing the fluoroscopic screen which is

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RÖNTGEN'S CLOSING YEARS

On March 3, 1896, the University of Würzburg conferred on Röntgen the honorary degree of Doctor of Medicine. In April he accepted the Royal Bavarian Order of the Crown, but declined to use the particle "von" which went with it [42]. In November of the same year he was awarded the Rumford Medal of the Royal Society. During the year he sacrificed this medal to Germany's demand for gold, but it is told by Margret Boveri that he later regretted his action. His second communication on the X-rays, of March 8, 1896 [43], deals with the discharge of electrified bodies by the X-rays. He noticed that air through which the rays had been passed retained this property of discharging electrified bodies for some time after it had been actually subjected to the rays. He extended his view that X-rays could arise in other materials besides glass, and he expressed the tentative opinion that any solid, and possibly liquids and gases as well, might serve as their origin. In his third communication (1897) [44] Röntgen dealt with a comparison of the intensity of radiation of two discharge tubes, and the value of the transparency of certain materials for rays produced from different tubes. All bodies are more transparent for the rays of a harder tube than for those of a softer one. He dealt also with the spontaneous hardening of tubes, and he stated that he had so far no evidence of the diffraction of the rays.

A survey of the whole of Röntgen's papers shows that his output fell rapidly after this period. During the years 1898 to 1921 he wrote only eight papers. It would seem that this result was associated with his transfer to Munich. In 1900 he accepted the post of Professor and Director of the Physical Institute in the University of that city. There is no clear explanation of his decision to go to Munich, but Dr. H. P. Bayon, who took a degree in Würzburg in 1902, informs me that official pressure was brought to bear on Röntgen by the Bavarian Government, which wanted his name to dignify the capital of that State [45]. Fräulein Boveri says that after 1900 fame and shyness raised a wall around Röntgen, through which an opening could be made occasionally, but which remained essentially intact until his death. The first Nobel Prize was awarded to him in 1901, and many other honours were showered upon him. During the years 1909 to 1913 he was not in good health, and he had two attacks of hæmoptysis.

Fräulein Boveri also mentions that the rumour had preceded him to Munich to the effect that he was difficult to get on with. To quote her words, she says that "if he did not agree with a person, he could be gruff and even rude". There seems little doubt that his rejection of the particle "von" to which he was entitled by the Bavarian honour which had been conferred on him, had not been well received in the court circles of Munich. Würzburg had been his spiritual home. Röntgen died on February 10, 1923, at the age of 77 years.

RÖNTGEN'S PLACE IN HISTORY

It is as yet too early to determine the place of Röntgen in the history of science. Glasser [46], who is an enthusiast, sums up his attitude to scientific investigation in the following passage: "The salient feature of Röntgen's work, which makes him an excellent representative of classicism, was his persistence and his critical honesty in making observations and measurements. He approached the solution of physical problems with great acuity and relentless thoroughness. Over and over again he worked out new control experiments in order to convince himself thoroughly of the absolute accuracy of the results which he had obtained, and with great scepticism he always warned against accepting any hypothesis which was not based upon sound experimental evidence. Therefore the results of his work which were published in his papers are distinguished by a rare reliability, combined with remarkable classical brevity and simplicity. Röntgen was an experimental physicist in the truest sense of the word."

On the other hand, these features alone without a succession of brilliant achievements do not indicate genius. Many outstanding physicists in this country consider that Röntgen's other work was not of the same order as that associated with his discovery of X-rays. It is undeniable that the achievements of men such as Sir William Crookes, Sir J. J. Thomson and Sir Ernest Rutherford were consistently more valuable in the development of atomic physics. The stage was set for the discovery of X-rays, and Röntgen was the actor chosen by fate to take the cue. Had he failed to do so, the discovery would certainly have been made by another. Even though this is admitted, the value of his work is in no way diminished, and his fame is secure as one of the greatest of mankind's benefactors during the nineteenth century.

now used in miniature radiography [33]. He was able to obtain an X-ray with a single interruption—he had indeed done this in April—and he was therefore the founder of X-ray cinematography. During the year 1896 alone MacIntyre published eighteen papers on X-rays. Sir Herbert Jackson chose potassium platino-cyanide as the salt which gives the best results, and in March 1894 he devised the first focus tube.

As an indication of the work which was done by these pioneers, the following list of those who contributed most to the literature of X-rays during the year 1896 will serve to show the extent, if not the quality, of the work of individual investigators: Battelli (Pisa)—12 papers (6 with Garbasso); Benoist and Hurmuzescu (Paris)—7 papers; Dufour (Lausanne)—6 papers; Edison—6 papers; Imbert and Bertin-Sans (Paris)—9 papers; Sir Oliver Lodge—15 papers; J. MacIntyre (Glasgow)—17 papers together with a joint paper; MacKenzie Davidson (Aberdeen)—5 papers; Mayer (New York)—4 papers; Meslin (Paris)—5 papers; Morton (New York)—8 papers; Oudin and Barthélemy (Paris)—4 papers; J. Perrin (Paris)—9 papers on the physical aspect; Poincaré (Paris)—7 papers on technical aspects; Pupin (New York)—6 papers; Righi (Bologna)—15 papers on technical aspects; Roiti (Italy)—8 papers on technical aspects; S. Rowland (London)—16 papers; Sella and Maiorana (Rome)—5 papers; Stenbeck (Stockholm)—5 papers; Stine (Chicago)—9 papers; Campbell Swinton (London)—20 papers; Silvanus P. Thompson—7 papers; E. Thomson (Lynn, Mass.)—16 papers; Sir J. J. Thomson—numerous papers; E. Villari (Italy)—17 papers.

Great credit is due to Sydney Rowland for his pioneer work on most aspects of X-rays. As early as the beginning of February 1896 the *British Medical Journal* appointed him as a Commissioner to report periodically on new developments. This he did very frequently for a long period. As a radiologist, his work was of a very high order. As an example of the progress which was being made it may be mentioned that in the case of Campbell Swinton's first X-ray of the hand, the exposure was about twenty minutes. By February 29 Rowland was obtaining a similar result with a 20 second exposure [34]. His first report to the *British Medical Journal* appeared on February 8. In May 1896 he published in London the first journal exclusively devoted to X-rays—the *Archives of Clinical Skiagraphy*. It was very successful, and in the following year it was enlarged under the joint editorship of himself and W. S. Hedley with the title *Archives of the Röntgen Ray*. About the same time were founded the *American X-ray Journal*, and the *Fortschritte auf dem Gebiete der Röntgenstrahlen*.

I have seen many of these early papers, but a brief mention can be made of only a few which have opened up new paths. In March 1896 Becher of Berlin introduced liquor plumbi subacet. into the stomach and intestines of recently killed guinea-pigs, and was able to demonstrate the contents by X-rays. He suggested that what was required for the human was a solution which does not damage the stomach, and which is opaque to the X-rays. This might be of use in cases of fistula. He also suggested the delimitation of the stomach by means of air. A little later Schrwald of Freiburg i. Breisgau showed that X-rays were absorbed by chlorine, bromine and iodine, and he suggested that one of these substances might be used to fill the internal organs. In the autumn of the same year Cannon of Harvard watched pearl buttons passing down the œsophagus of a dog, and he gave capsules of bismuth subnitrate to frogs. In July 1896 MacIntyre successfully located a stone in the kidney by X-rays. Even scientists were not completely free from the optimism which was displayed by the popular Press. In February 1896 it was reported from America that after the shadow of a bone was projected with X-rays on the brain of a dog, he immediately became hungry [35].

From the earliest days there are suggestions regarding the use of X-rays in treatment. On February 1, Lyon had a letter in the *Lancet* in which he suggested that pulmonary tuberculosis might be treated in this way, but three weeks later he reported that he had experimented with cultures of diphtheria and tubercle bacilli, and that the X-rays had no germicidal effect [36]. On February 29 Professor Délépine reported that with Professor Schuster he had carried out experiments to test the effect of X-rays on the cholera vibrio. *Bacillus coli* and *Bacillus typhosus* respectively; all results were negative [37]. The first successful use of the rays in treatment was made by L. Freund of Vienna in November 1896. The patient was a girl with a pigmented birthmark. From then on numerous cases were treated by various modifications of the method. There were many reports of attempts to treat chronic fatal diseases with X-rays. For example Despeignes [38] of Lyons claimed that he had obtained marked improvement of a cancer of the stomach by two half-hour sittings daily for two or three weeks. Early reports of risks to operators came from Edison's laboratory. Daniel [39] found that in a patient who had an exposure of one hour for an X-ray of the skull, there resulted an area of epilation of the scalp, two inches in diameter. In July 1896 Marcuse reported an experiment carried out on a young man, who received one or two doses (each of five to ten minutes) daily for four weeks on his scalp. Alopecia was followed by erythema, conjunctivitis, and then excoriation of skin over the back and chest [40]. It was soon realized that the dermatitis resulting from X-rays was very intractable. The years have brought their victims, and at least two books have been devoted to biographies of these martyrs to science. It is worthy of note that Röntgen, for purely scientific reasons, did most of his observations from inside a lead cabinet. So far as I am aware he never suffered any ill-effects from the rays.

Davis and Keen of Philadelphia made the first X-ray of a pregnant woman in February 1896 [41].

During these early days a number of advances were made in the more mechanical aspects of the plant. Tube holders were a difficulty. There are some grounds for thinking that the Italians were the first to use the rays in warfare, but certainly they were used first on a considerable scale by the British in the Nile expedition of 1896.

RÖNTGEN'S CLOSING YEARS

On March 3, 1896, the University of Würzburg conferred on Röntgen the honorary degree of Doctor of Medicine. In April he accepted the Royal Bavarian Order of the Crown, but declined to use the particle "von" which went with it [42]. In November of the same year he was awarded the Rumford Medal of the Royal Society. During the war he sacrificed this medal to Germany's demand for gold, but it is told by Margret Boveri that he later regretted his action. His second communication on the X-rays, of March 8, 1896 [43], deals with the discharge of electrified bodies by the X-rays. He noticed that air through which the rays had been passed retained this property of discharging electrified bodies for some time after it had been actually subjected to the rays. He extended his view that X-rays could arise in other materials besides glass, and he expressed the tentative opinion that any solid, and possibly liquids and gases as well, might serve as their origin. In his third communication (1897) [44] Röntgen dealt with a comparison of the intensity of radiation of two discharge tubes, and the value of the transparency of certain materials for rays produced from different tubes. All bodies are more transparent for the rays of a harder tube than for those of a softer one. He dealt also with the spontaneous hardening of tubes, and he stated that he had so far no evidence of the diffraction of the rays.

A survey of the whole of Röntgen's papers shows that his output fell rapidly after this period. During the years 1898 to 1921 he wrote only eight papers. It would seem that this result was associated with his transfer to Munich. In 1900 he accepted the post of Professor and Director of the Physical Institute in the University of that city. There is no clear explanation of his decision to go to Munich, but Dr. H. P. Bayon, who took a degree in Würzburg in 1902, informs me that official pressure was brought to bear on Röntgen by the Bavarian Government, which wanted his name to dignify the capital of that State [45]. Fräulein Boveri says that after 1900 fame and shyness raised a wall around Röntgen, through which an opening could be made occasionally, but which remained essentially intact until his death. The first Nobel Prize was awarded to him in 1901, and many other honours were showered upon him. During the years 1909 to 1913 he was not in good health, and he had two attacks of hæmoptysis.

Fräulein Boveri also mentions that the rumour had preceded him to Munich to the effect that he was difficult to get on with. To quote her words, she says that "if he did not agree with a person, he could be gruff and even rude". There seems little doubt that his rejection of the particle "von" to which he was entitled by the Bavarian honour which had been conferred on him, had not been well received in the court circles of Munich. Würzburg had been his spiritual home. Röntgen died on February 10, 1923, at the age of 77 years.

RÖNTGEN'S PLACE IN HISTORY

It is as yet too early to determine the place of Röntgen in the history of science. Glasser [46], who is an enthusiast, sums up his attitude to scientific investigation in the following passage: "The salient feature of Röntgen's work, which makes him an excellent representative of classicism, was his persistence and his critical honesty in making observations and measurements. He approached the solution of physical problems with great acuity and relentless thoroughness. Over and over again he worked out new control experiments in order to convince himself thoroughly of the absolute accuracy of the results which he had obtained, and with great scepticism he always warned against accepting any hypothesis which was not based upon sound experimental evidence. Therefore the results of his work which were published in his papers are distinguished by a rare reliability, combined with remarkable classical brevity and simplicity. Röntgen was an experimental physicist in the truest sense of the word."

On the other hand, these features alone without a succession of brilliant achievements do not indicate genius. Many outstanding physicists in this country consider that Röntgen's other work was not of the same order as that associated with his discovery of X-rays. It is undeniable that the achievements of men such as Sir William Crookes, Sir J. J. Thomson and Sir Ernest Rutherford were consistently more valuable in the development of atomic physics. The stage was set for the discovery of X-rays, and Röntgen was the actor chosen by fate to take the cue. Had he failed to do so, the discovery would certainly have been made by another. Even though this is admitted, the value of his work is in no way diminished, and his fame is secure as one of the greatest of mankind's benefactors during the nineteenth century.

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